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3D Bioprinting Patentable Subject Matter Boundaries

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3D BIOPRINTING PATENTABLE SUBJECT MATTER BOUNDARIES

*Tabrez Y. Ebrahim**

ABSTRACT

3D bioprinting combines emerging 3D printing technologies with synthetic biology. The promise of 3D bioprinting technology is to fabricate organs for transplantation, treat burn victims with *in vivo* skin repair, and create wearable microbiomes. 3D bioprinting can successively build, repair, or reproduce living human cells. This capability challenges eligible subject matter doctrine in U.S. patent law because the law has no bright-line standard for patent eligibility for nature-based products. As 3D bioprinting technologies mature, U.S. patent law will need to respond to situations where living and nonliving worlds merge. This Article proposes a “Mixed-Scanned-Transformed” standard to supplement U.S. patent law’s “markedly different characteristics” examination of nature-based products. The markedly different standard arose from the *Chakrabarty* case in 1980 and is most recently informed by the *Myriad* case in 2013, but neither case involved merging living and nonliving worlds. By applying this newly proposed standard, 3D bioprinted materials would likely be upheld as patentable subject matter. The proposed “Mixed-

* Tabrez Y. Ebrahim is a Patent Attorney at Bracewell LLP in Houston, Texas, an Adjunct Professor and Corporate Fellow at the University of Houston-Downtown Davies College of Business, and a Member of the Baylor College of Medicine Center for Medical Ethics & Health Policy. He graduated from the University of Texas at Austin with a BS in Mechanical Engineering (with High Honors), from Stanford University with a MS in Mechanical Engineering, from Northwestern University with a JD and a MBA, and from the University of Houston Law Center with a LL.M. in Intellectual Property & Information Law.

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Scanned-Transformed” standard and proposed clarity on what is *not* a “human organism” will allow U.S. patent law to become more bright-line towards 3D bioprinting inventions.

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INTRODUCTION

The 3D printing revolution has moved beyond consumer and industrial uses and into biotechnology. This new technology produces living biological cells, tissues, and organs by clicking a computer mouse. Just as digitization of physical objects has enabled rapid production of customized objects,¹ the confluence of tissue engineering, synthetic biology, and additive manufacturing can yield tailor-designed biomaterials and organs. This new technology applies 3D printing's ability to modify virtual physical objects in digital computer-aided design (CAD) files towards translating medical images of human anatomy into print-ready Bio-CAD files. This new phenomenon is termed 3D bioprinting.

3D printing has blurred the line between the digital and physical worlds.² 3D bioprinting as a subset of 3D printing similarly blurs the digital and physical and also blurs the line between living and nonliving worlds. As 3D bioprinting has emerged from the research laboratory and into a commercial reality,³ it is eroding the boundaries separating human from nonhuman and products of nature from printed products of nature. These boundaries are fuzzy and inadequately defined. The transformative technology of 3D bioprinting magnifies the unclear patentable subject matter boundaries of biotechnology. The convergence of living and nonliving worlds with the emergence of 3D bioprinting requires assessing

1. Deven R. Desai & Gerard N. Magliocca, *Patents, Meet Napster: 3D Printing and the Digitization of Things*, 102 GEO. L.J. 1691, 1697–99 (2014).

2. See generally Daniel Harris Breaun, *Patenting Physibles: A Fresh Perspective for Claiming 3D-Printable Products*, 55 SANTA CLARA L. REV. 837 (2015); Lucas S. Osborn, *Regulating Three-Dimensional Printing: The Converging Worlds of Bits and Atoms*, 51 SAN DIEGO L. REV. 553, 558–62 (2014) (discussing that the advent of computer technology and developments in 3D printing technology create struggles with how to apply the law of atoms to the computer world of “bits” of ones and zeros).

3. CHRISTOPHER BARNATT, 3D PRINTING 177–84 (2d ed. 2014).

what defines the patentable subject matter boundaries and the legal standards that determine what can enter those boundaries.

This Article represents a proposal for evaluating the limits of patentable subject matter necessitated by 3D bioprinting technology under U.S. patent law. The emerging phenomena of 3D bioprinting challenges the dividing line between living and nonliving and necessitates that the patent system respond to better define patentable subject matter boundaries. This Article fills a gap in legal scholarship by addressing how 3D bioprinting stresses patentable subject matter doctrine. To date, legal scholars have assumed that the same assessment for 3D printing applies to 3D bioprinting. This Article challenges that assumption by demonstrating that the long-standing uncertainties in the law of patentable subject matter with biotechnological inventions⁴ are further stressed with the emergence of 3D bioprinting technology and its applications. This Article's guiding theme is that a clearer standard will lead to clearer patenting in 3D bioprinting.

This Article explores the ways that the U.S. patent system will need to respond to the advent of 3D bioprinting. It proceeds as follows: after introducing an overview of 3D printing, Part I describes the foundational principles of 3D bioprinting technology and gives examples of applications. This Part introduces Bio-CAD files that can translate medical images into digital models, can modify living elements *in silico*, or can introduce nonliving elements with living elements *in silico*.

Part II of this Article suggests a lack of a clear standard for patentable subject matter in biotechnology through analyses of cases, United States Patent & Trademark Office (USPTO) examination guidance, and discussion of patent law in the Leahy-Smith America Invents Act (AIA). Beginning with the early U.S. patent law cases concerning the nature and non-nature distinction, Part II discusses decades of U.S. Supreme Court and Federal Circuit cases that entangled patentable subject matter in uncertainty. More specifically, it introduces the origins of the markedly different characteristics standard, which serves as the current foundation for USPTO examination of nature based products. Part II concludes with an analysis of the statutory construction and legislative history of the AIA's vague phrase "human organism," which obfuscates patentable subject matter of nature based products.

Part III applies the markedly different characteristics standard and the human organism exception to each facet of 3D bioprinting. It concludes that processed 3D bioprinted materials would likely be patentable subject matter. It determines that post-processed and integrated

4. Dan L. Burk, *Dolly and Alice*, 2 J. L. & BIOSCI. 606 (2015).

3D bioprinted materials may or may not be patentable subject matter depending on the reach of the human organism exception. It suggests that 3D bioprinting inventions can sidestep the human organism limitation when the 3D bioprinted object is not fully biological but is either a mix of biological and artificial elements or is a modified replica of a product of nature. Part III also addresses why certain 3D bioprinting inventions that merge living and nonliving elements are not patentable subject matter. It investigates the following questions: Should a slightly modified replication of a living tissue become patent eligible when it is 3D bioprinted in a less than fully living state? What does it mean to be “human” within 3D bioprinting? How does patent law doctrine address a mixed biological–mechanical 3D bioprinted object? Should 3D bioprinted wearable microbiomes that nourish the skin and repair damaged tissues be considered patentable subject matter? Where does the notion of 3D bioprinting stop, and where does the nonliving, mechanical world begin?

Part IV examines how patent law can respond to the need to have a clearer standard for patentable subject matter with the emergence of 3D bioprinting. Unless a more bright-line standard is provided, questions on patent eligibility will abound as 3D bioprinting proliferates. In responding to the impact of 3D bioprinting on patent law, this Article proposes a novel claim: Because 3D bioprinting is rapidly evolving towards fusing living and nonliving worlds, a more bright-line standard is needed to overcome the shortcomings of the markedly different characteristics standard. This Part suggests a “Mixed-Scanned-Transformed” (MST) standard to supplement patent law’s markedly different characteristics examination of nature-based products. This Part addresses fitting the proposed MST standard within patent law’s uniformity principle. Part IV concludes with policy implications of a clearer standard for patentable subject matter. It argues that a more bright-line standard for patentable subject matter would lead to clearer patenting, provide greater investment impetus, and reduce downstream litigation burdens with emerging 3D bioprinting.

I. OVERVIEW OF 3D BIOPRINTING

3D bioprinting combines synthetic biology with 3D printing in a synergistic way to automate generation of living cells.⁵ 3D bioprinting is a subset of 3D printing, and pairs concepts of 3D printing with synthetic

5. Mark A. Lemley, *IP in a World Without Scarcity*, 90 N.Y.U. L. REV. 460, 478 (2015); Phoebe H. Li, *3D Bioprinting Technologies: Patents, Innovation, and Access*, 6 L. INNOVATION & TECH. 282 (2015); Timo Minssen & Marc Mimler, *Patenting Bioprinting-Technologies in the US and Europe: The 5th Element in the 3rd Dimension*, in 3D PRINTING, INTELLECTUAL PROPERTY & INNOVATION – INSIGHTS FROM LAW AND TECHNOLOGY (Rosa Maria Ballardini et al. eds., 2017).

biology to produce biological materials.⁶ 3D bioprinting refers to the extrusion of a biological ink layer-by-layer,⁷ such that simultaneously deposited live cells and growth factors produce a construction to grow human cells or tissues.⁸

The same technological foundations of 3D printing apply to 3D bioprinting. The novelty in 3D bioprinting is the printed product is biological in nature, comprised of complex tissues, and has natural architecture. The benefits of 3D bioprinting are the provision of real time potential healthcare treatments, the measuring of efficacy and safety, and the creation of more natural, cell-to-cell interactions compared to traditional 2D printing methods.⁹

However, unlike 3D printing, where materials are easier to print and the printers are rapidly being adopted by the masses,¹⁰ 3D bioprinting advancements have been severely limited by printable biological materials that do not yet fully mimic nature.¹¹ The successful future of 3D bioprinting depends on optimizing the biomaterial properties so that printed cells can remain viable for extended time periods to properly organize and function.¹²

A. Overview of 3D Printing

3D printing is a technology that enables the creation and replication of a three-dimensional, solid object.¹³ 3D printing utilizes an “additive

6. Jasper L. Tran, *To Bioprint or Not To Bioprint*, 17 N.C. J. L. & TECH. 123, 129 (2015).

7. Adam E. Jakus et al., *Advancing the Field of 3D Biomaterial Printing*, BIOMED. MATER., January 8, 2016, at 1.

8. Vivian K. Lee et al., *3D Bioprinting and 3D Imaging for Stem Cell Engineering*, in BIOPRINTING IN REGENERATIVE MEDICINE 33 (Kursad Turksen ed., 2015).

9. David Sher, *The Top 15 Bioprinters*, 3D PRINTING INDUSTRY (Aug. 26, 2015), <https://3dprintingindustry.com/news/top-10-bioprinters-55699/> [<https://perma.cc/VU85-4VSX>].

10. Stratasys Direct Manufacturing, *3D Printing Materials: Choosing the Right Material for Your Application 3* (2015) (unpublished white paper), https://www.stratasysdirect.com/content/white_papers/STR_7463_15_SDM_WP_3D_MATERIALS.PDF [<https://perma.cc/6N7P-WW4L>] (stating that 3D printing materials achievements have skyrocketed over the last five to ten years and that 3D printing processes today can create prototypes and end-use production parts in hundreds of plastic and metal materials).

11. Helena N. Chia & Benjamin M. Wu., *Recent Advances in 3D Printing of Biomaterials*, J. BIOLOGICAL ENGINEERING, Mar. 1, 2015, at 2–3 (clarifying that advances in 3D printing machine capabilities have not yet translated completely with biomaterials but suggesting that advances in digitized medical imaging data and integration with patient-specific medical imaging data with 3D printing will allow for printing of tissue engineering grafts that will match precisely a patient’s contours).

12. See Jakus et al., *supra* note 7, at 5 (discussing that developments in 3D bioprinting materials have been limited by tunability, or the ability to effectively change the formulation and properties of the biological material, and printability, or the ability to consistently 3D print a material in a defined, multi-layer construct).

13. Tabrez Y. Ebrahim, *3D Printing: Digital Infringement and Digital Regulation*, 14 NW. J. TECH. & INTELL. PROP. 37, 42 (2016).

manufacturing” process to build products by adding many very thin layers of material, layer on top of layer.¹⁴ Each layer produced by an additive manufacturing process is, therefore, a cross-section of a part. The content of the deposited material is built on top of the preceding layer and fused to the underlying layer until an entire object emerges at the end of the process.¹⁵

The brain of a 3D printing operation is an electronic CAD file, which serves as a blueprint model for producing the output product.¹⁶ This CAD file can be created from 3D modeling software, from scanning a 3D object, or from tweaking a scanned object in modeling software. 3D printing offers the ability to make a physical object using an electronic file, which contains the digital printing instructions. In essence, a 3D printing machine enables users to turn a digital blueprint into a physical object with the press of a button.¹⁷

B. *Technological Foundations of 3D Bioprinting*

3D printing is a technology that has been in existence since the 1980s, but 3D bioprinting is just beginning to emerge from the research laboratory and into the marketplace.¹⁸ Just like a 3D printer can print a physical object based on a digital CAD file,¹⁹ a 3D bioprinter can print three-dimensional biological materials.²⁰ 3D bioprinting combines the engineering principle of rapid prototyping with the science of tissue engineering in a controlled environment to accelerate cell adhesion,

14. Elizabeth Matias & Bharat Rao, *3D Printing: On Its Historical Evolution and the Implication for Business*, 2015 PROCEEDINGS OF PICMET '15: MGMT. OF THE TECH. AGE 551, 551 (2015).

15. See Osborn, *supra* note 2, at 559.

16. Michael Weinberg, *It Will Be Awesome if They Don't Screw Up: 3D Printing, Intellectual Property, and the Fight Over the Next Great Disruptive Technology* 3–4 (Nov. 2010) (unpublished white paper), <https://www.publicknowledge.org/files/docs/3DPrintingPaperPublicKnowledge.pdf> [<https://perma.cc/5EY2-P7FH>] (explaining that the CAD design process eliminates the need to design physical prototypes out of other materials not needed for the object, and that a designer can use a CAD program to create and manipulate a virtual model that is saved to a file).

17. *Id.*

18. See BARNATT, *supra* note 3, at 19.

19. Lucas Osborn & Timothy R. Holbrook, *Digital Patent Infringement in an Era of 3D Printing*, 48 U.C. DAVIS L. REV. 1319, 1329 (2015) (discussing that 3D printing builds an object up layer-by-layer using a print head that emits a molten material to print a first layer, after which the print head moves up to place the second layer upon the first layer, continuing the process until the object is complete; further defining that a three-dimensional print requires instructions to a 3D printer in the form of a CAD file, which is a digital representation of the physical object and can be created either from scratch using a computer program or by scanning a physical object with a scanner).

20. Gabriela I. Coman, *3-D Bioprinting: 5 Things Medical Device Cos. Should Know*, LAW360 (Feb. 18, 2016), <https://www.law360.com/articles/760558/3-d-bioprinting-5-things-medical-device-cos-should-know> [<https://perma.cc/C4SF-XQ34>].

proliferation, and differentiation to produce functional, living tissues.²¹ 3D bioprinting's ability to produce biological tissues and organs subject it to a higher scrutiny than 3D printing.²² Another difference from 3D printing is that 3D bioprinting processes are more complex, take greater time to complete, and require more steps. For each of these reasons, the overview of 3D bioprinting technology will be more in-depth than the overview of 3D printing technology.

3D bioprinting beneficially impacts healthcare through implantable and non-implantable medical devices and cost-effective customizable devices in three new ways.²³ First, 3D bioprinting enables computer-controlled manufacturing²⁴ of living human tissue through layered deposition of material.²⁵ Second, 3D bioprinting promotes nature's magic by fusing together biological cells during the 3D bioprinting process.²⁶ Third, 3D bioprinting can combine nonliving materials with living materials in bio-inspired printing processes to produce functional devices in a customized fashion,²⁷ which can also be used in non-healthcare applications.

21. Silke Wust et al., *Controlled Positioning of Cells in Biomaterials: Approaches Toward 3D Tissue Printing*, 2 J. FUNCT. BIOMATER. 119, 121–44 (2011) (defining 3D bioprinting as the production of complex living and non-living biological products by placing proteins, peptides, DNA, cells, hormones, or ECM molecules together with biomaterials through seeding cells onto scaffolds or encapsulating cells into porous hydrogels for nutrient support to replicate living structures to nanostructure scale).

22. See Tran, *supra* note 6, at 147–50.

23. CELESTE A. LETOURNEAU ET AL., 3D PRINTING OF MEDICAL DEVICES: WHEN A NOVEL TECHNOLOGY MEETS TRADITIONAL LEGAL PRINCIPLES 4 (Colleen Davies et al. eds., 1st ed., 2015).

24. David Chimene et al., *Advanced Bioinks for 3D Printing: A Materials Science Perspective*, 44 ANNALS OF BIOMEDICAL ENGINEERING 2091 (2016).

25. Ali Bakshinejad & Roshan M. D'Souza, *A Brief Comparison Between Available Bio-printing Methods*, GREAT LAKE BIOMEDICAL CONFERENCE (Feb. 17, 2015), <https://pdfs.semanticscholar.org/f9cb/1d43990f14eaf6f3a9ed632b432cd050a05c.pdf> [<https://perma.cc/3TRM-EDAN>] (categorizing the biological aspect of 3D bioprinting either as: 1) scaffold based printing, where a skeleton of organ/tissue geometry is printed using biomaterials, the scaffold is subsequently populated with living cells to colonize the scaffold, and finally the scaffold resolves into the system, and 2) scaffold-free printing, where the living cells are deposited directly into the substrate, resulting in automatically generated structures through cell signaling; further describing the bioprinting process itself as either being: 1) laser-assisted bioprinting, where a focused laser pulse causes local vaporization of an energy absorbing layer, resulting in a bioink droplet based on the energy of the pulse, or 2) laser-free bioprinting, where inkjet printing of a bioink occurs through actuating a printhead either thermally or piezoelectrically, or alternatively through a robotic dispensing mechanism resulting in a continuous stream of bioink).

26. See BARNATT, *supra* note 3, at 179–81; Lydialyle Gibson, *Building Towards a Kidney*, HARVARD MAGAZINE, Jan.–Feb. 2017, at 38, 40–41 (describing the use of 3D bioprinting technology to lay the foundation of a biological building block in the form of subcomponent of a nephron that serves as a modular unit towards creating multi-layer tissue, which can be applied towards screening of new drugs).

27. Neri Oxman, *Variable Property Rapid Prototyping*, 6 VIRTUAL & PHYSICAL PROTOTYPING 3, 8–13 (2011) (demonstrating Variable Property Modeling to 3D print bio-inspired natural structures

Simply put, the 3D bioprinting process includes modeling and design of blueprint instructions, depositing material by printing, and maturing of the biological material with potential implantation. The process of 3D bioprinting is comprised of three steps: First, a computer model or a scanned image creates a digital blueprint of the object to be printed on the computer; second, living cells are mixed with a gel to create bio-inks for the 3D bioprinter; and third, the 3D bioprinter deposits the bio-ink through printing nozzles onto a platform to produce the final product.²⁸ In effect, the three steps of 3D bioprinting can be characterized as pre-processing or development of blueprints of organs, processing or actual organ printing, and post-processing or accelerated organ maturation.²⁹

In the first 3D bioprinting step, pre-processing, neuroimaging by either magnetic resonance imaging (MRI) or computed tomography (CT) converts medical imaging data into virtual 3D models of internal organs, which can be edited in a 3D modeling program.³⁰ The mapping of a human organ via MRI or CT scan converts a medical image into a bio-computer aided design (Bio-CAD) file, which allows for visualization of anatomic structures, differentiation of tissue types, and generation of a computational tissue model.³¹ The Bio-CAD file, which is the starting point for 3D bioprinting, creates or modifies a software representation of anatomic and geometric information of the 3D bioprinted tissue or organ.³² Bio-CAD files can also make it easy for the viewer to visualize a 3D bioprinted object for use in a medical application or procedure.³³

with graduated and varied properties by use of organic, inorganic, or multifunctional composites, such as shells, pearls, corals, teeth, wood, silk, horn, collagen, and muscle fibers, for use in industrial and architectural applications).

28. Craig C. Martin & Sara Tonnie Horton, *Patent Eligibility of 3D Printed Organs Will Soon Be an Issue*, TODAY'S GENERAL COUNSEL, June–July 2014, at 36.

29. Vladimir Mironov et al., *Organ Printing: Computer-Aided Jet-Based 3D Tissue Engineering*, 22 TRENDS IN BIOTECH. 157 (2004) (describing that preprocessing primarily deals with the development of a Computer-Aided Design, or CAD, blueprint files of a specific organ, processing refers to actual CAD-printing or layer-by-layer placement of the cells or cell aggregates, and postprocessing concerns the perfusion of printed organs and their biomechanical conditioning to accelerate organ maturation; further predicting that developments with such steps and with 3D bioprinting will yield, in the 21st century, cell and organ 3D bioprinters that are as broadly used as biomedical research tools, as was the electron microscope in the 20th century).

30. Jason S. Naftulin et al., *Streamlined, Inexpensive 3D Printing of the Brain and Skull*, PLOS ONE, 2015.

31. Ahmed Munaz et al., *Three-Dimensional Printing of Biological Matters*, in JOURNAL OF SCIENCE: ADVANCED MATERIALS AND DEVICES 1, 2 (2016).

32. W. Sun et al., *Bio-CAD Modeling and Its Applications in Computer-Aided Tissue Engineering*, 37 COMPUTER-AIDED DESIGN 1110, 1112 (2005).

33. *3D Prints in Medicine*, U.S. DEP'T OF HEALTH AND HUM. SERVICES – NAT'L INST. OF HEALTH: NIH 3D PRINT EXCHANGE, <http://3dprint.nih.gov/about/medicine> [<https://perma.cc/TYV5-6LXX>] (promoting itself as a trusted digital repository of digital 3D models for medical applications that are compatible with 3D printers in its Terms & Conditions).

In the second 3D bioprinting step, processing, spheroids of living cells are dispensed by the 3D bioprinting and deposited layer-by-layer onto hydrogels, which act like a biopaper to collect and maintain cell placement, and aid in tissue fusion and maturation.³⁴ The conceptual framework for the processing step of 3D bioprinting is that spheroids will be precisely dispensed onto specified hydrogel biopapers, such that tissues and organs will eventually self-assemble and self-organize by perfusion.³⁵ The ability to replicate nature inside of a 3D bioprinter challenges the analysis of natural processes, products of nature, and transformations from nature in U.S. patent law.

In the third 3D bioprinting step, post-processing, 3D bioprinted tissue spheroids fuse by assembling, compacting, and maturing into functional tissue.³⁶ The post-processing step includes placing the 3D bioprinted structure into an incubator for maturation, testing, monitoring, and preservation.³⁷ The ability to replicate nature during 3D bioprinting maturation processes raises concerns under U.S. patent law concerning transformations from nature.

C. Applications: Organ Transplantation, In Vivo Skin Repair, Wearable Microbiomes

3D bioprinting technology is capable of fabricating tissues *in vitro* or *in situ*, and researchers have produced 3D bioprinted aortic valves, bones, cartilage, ears, eyes, heart tissue, kidneys, skin, windpipes, and vasculature.³⁸ An emerging research application of 3D bioprinting is the

34. Natalie M. Kerestes, *Bioprinting: Is This the Solution to the Organ Transplant Crisis?*, U. OF TOLEDO MASTERS AND DOCTORAL PROJECTS, Paper 534 at 9 (2012).

35. Vladimir Mironov et al., *Organ Printing: Tissue Spheroids as Building Blocks*, 30 BIOMATERIALS 2164 (2009) (suggesting that self-assembled tissue spheroids are an alternative to scaffold-based tissue engineering and, therefore, permit automation, scalability, reproducibility, precision, and high cell density).

36. Rodrigo A. Rezende et al., *Three-Dimensional Bioprinting of Human Organs: Phases and Concepts*, CONGRESSO LATINO AMERICANO DE ÓRGÃOS ARTIFICIAIS E BIOMATERIAIS, Aug. 2015.

37. Armando Salim Munoz-Abraham et al., *3D Printing of Organs for Transplantation: Where Are We and Where Are We Heading?*, 3 CURR. TRANSPL. REP. 9, 96 (2016); Rodrigo A. Rezende et al., *Development of a Bioreactor by Computational Fluid Dynamics Simulations for the Maturation of 3D Printed Organs by Rapid Prototyping*, 32 CHEMICAL ENGINEERING TRANSACTIONS 1153 (2013).

38. See, e.g., Sean V. Murphy & Anthony Atala, *3D Bioprinting of Tissues & Organs*, 32 NATURE BIOTECH. 773 (2014); Evan R. Youngstrom, *3D Printing and Healthcare: Will Laws, Lawyers, and Companies Stand in the Way of Patient Care?*, 6 PACE. INTELL. PROP. SPORTS. & ENT. L.F. 91 (2016). In molecular and cellular biology, *in situ* is the intermediate classification between *in vivo* and *in vitro*. *In vivo* means investigating something within its living context and *in vitro* refers to something taken out of its context, whereas *in situ* refers to looking at something in its natural context but perhaps not under natural conditions. In sum, *in vivo* means “in the living” and *in situ* means “on site.”

production of bioprosthetic ovaries.³⁹ This Article focuses on three applications of 3D bioprinting—organ transplantation, *in vivo* skin repair, and wearable microbiomes—and how each can challenge patentable subject matter principles.

One application of 3D bioprinting is organ transplantation. 3D bioprinting utilizes tissue engineering principles to replace damaged tissues, restore malfunctioning organs, and permit full organ transplantation by mimicking native tissues.⁴⁰ The application of 3D bioprinting towards producing tissues and organs involves either the use of a particular patient's own cells or implantation of 3D bioprinted materials to help regenerate organs.⁴¹ Organ fabrication via 3D bioprinting is becoming a commercial substitute to address the organ donation shortage in the U.S.⁴² For example, 3D bioprinting research and development is progressing towards the first replacement heart developed from a patient's own cells.⁴³ 3D bioprinting promises to decrease the number of patients left waiting for organ transplants, reduce the number of deaths due to organ inaccessibility, and eradicate organ rejection and immunosuppression drugs, thereby revolutionizing medicine.⁴⁴

Another application of 3D bioprinting is *in vivo* skin repair. 3D bioprinting can be utilized for skin repair, skin substitution, and skin reengineering, so that the 3D bioprinted skin equivalents can rapidly and completely restore skin function.⁴⁵ While still in its infancy, *in situ* 3D bioprinting can form skin with properties similar to healthy skin, and can

39. See generally Monica M. Laronda et al., *A Bioprosthetic Ovary Created Using 3D Printed Microporous Scaffolds Restores Ovarian Function in Sterilized Mice*, NATURE COMM., 2017 (discussing research aimed at creating functional 3D bioprinted replacement ovaries to help restore fertility in women cancer survivors).

40. Amer B. Dabahneh & Ibrahim T. Ozbolat, *Bioprinting Technology: A Current State-of-the-Art Review*, 136 J. OF MANUFACTURING SCI. & ENGINEERING 061016-1 (2014) (describing that 3D bioprinting produces human organs by patterning and assembling living and nonliving materials with a prescribed layer-by-layer stacking organization).

41. Anthony Atala, *Printing a Human Kidney*, TEDTALKS (Mar. 2011), https://www.ted.com/talks/anthony_atala_printing_a_human_kidney?language=en [<https://perma.cc/MUY5-VZ6F>].

42. MICHELLE GOODWIN, BLACK MARKETS: THE SUPPLY AND DEMAND OF BODY PARTS 7, 40–41 (2006) (stating that each day, eighteen people on an organ waitlist die before ever receiving the anticipated organ and are replaced with 110 persons will enter that list by end of the day, and that this list continues to rise each year; further suggesting that while the demand drastically overshadows supply, not all organ donations are viable because an organ donation does not always translate into a successful organ transplant); Jeremy Thomas Harbaugh, *Do You Own Your 3D Bioprinted Body? Analyzing Property Issues at the Intersection of Digital Information and Biology*, 41 AM. J. L. & ETHICS 168, 173 (2015) (describing a current waiting list of near 125,000 in the U.S.).

43. Cindy Glass, *3D-Printed Organs Are a Heartbeat Closer to Reality*, AUTODESK (June 20, 2015), <https://lineshapespace.com/3d-printed-organs-bioficial-heart/> [<https://perma.cc/2353-D7SS>].

44. See Kerestes, *supra* note 34, at 12–13.

45. Deepthi Singh et al., *3D Printing of Scaffold for Cells Delivery: Advances in Skin Tissue Engineering*, POLYMER, 2016, at 4, 8–13.

treat skin lesions and heal wounds.⁴⁶ 3D bioprinting techniques can treat burn victims as an *in vivo* alternative to skin grafts, or can offer cosmetic face printing to mimic celebrities' faces, re-bioprinting one's younger self to appear perpetually young or replacing unwanted layers of flesh.⁴⁷ 3D bioprinting has attracted interest from the skincare industry, including two major commercialization partnerships.⁴⁸ The L'Oreal-Organovo partnership aims to develop 3D bioprinted skin tissues⁴⁹ and develop automated testing of cosmetic skin products.⁵⁰ The BASF-Poietis partnership proposes to 3D bioprint the closest equivalent to the original physiological tissue of human skin and in doing so, support the development and testing of cosmetic bioactives for skin care applications.⁵¹ Moreover, consumer-goods giant Procter & Gamble has invested in 3D bioprinting artificial skin research and development, manufacturing, and test programs to test the efficacy and toxicity of its new cosmetic, beauty, dermatology, and skin care products.⁵²

Yet another application for 3D bioprinting is wearable microbiomes. In addition to healthcare benefits, 3D bioprinting has clothing applications in the form of wearable microbiomes, which can also support, control, and manipulate living organisms in wearable clothing designs.⁵³ Inspired by nature, wearable microbiomes are produced by 3D bioprinted, wearable natural materials that incorporate and contain living organisms in close proximity to skin in a symbiotic relationship ideal for new spacesuit

46. Rúben F. Pereira et al., *Advanced Biofabrication Strategies for Skin Regeneration and Repair*, NANOMEDICINE, 2013, at 12–14.

47. See BARNATT, *supra* note 3, at 190, 194–96.

48. Andy Extance, *Cosmetics Deals Push Skin 3D Bioprinting*, CHEMISTRY WORLD (Sept. 24, 2015), <https://www.chemistryworld.com/news/cosmetics-deals-push-skin-3d-bioprinting/8977.article> [<https://perma.cc/HY3G-995W>]; *BASF and Poietis Sign a Research and Development Agreement on 3D Bioprinting Technology for Advanced Skin Care Applications*, BASF (July 10, 2015), <https://www.basf.com/en/company/news-and-media/news-releases/2015/07/p-15-281.html> [<https://perma.cc/2353-D7SS>]; *L'Oreal USA Announces Research Partnership with Organovo to Develop 3-D Bioprinted Skin*, ORGANOVO (May 5, 2015), <http://ir.organovo.com/phoenix.zhtml?c=254194&p=irol-newsArticle&ID=2129344> [<https://perma.cc/4S6R-8TZT>].

49. *Organovo Investor Presentation*, ORGANOVO 21 (Nov. 2015), <http://organovo.com/wp-content/uploads/2015/11/Organovo-Investor-Presentation-1115.pdf> [<https://perma.cc/JQD4-7B29>].

50. Caroline Winter, *L'Oreal's Plan to Start 3D Printing Human Skin*, BLOOMBERG (May 18, 2015), <http://www.bloomberg.com/news/articles/2015-05-18/l-oreal-s-plan-to-start-3d-printing-human-skin> [<https://perma.cc/52TH-3ZLG>].

51. Simon Cosimo, *BASF and Poietis Enter R&D Agreement for 3D Bioprinting and Skin Care*, 3DERS (July 12, 2015), <http://www.3ders.org/articles/20150712-basf-and-poietis-enter-rd-agreement-for-3d-bioprinting-and-skin-care.html> [<https://perma.cc/9ZPA-KRSZ>].

52. Andrew McDougall, *P&G Sets Off on 3D Bioprinted Skin Research Project*, COSMETICS DESIGN (June 3, 2015), <http://www.cosmeticsdesign-europe.com/Formulation-Science/P-G-sets-off-on-3d-bioprinted-skin-research-project> [<https://perma.cc/DLG8-FQAK>].

53. Carrie Wyman, *Neri Oxman's 3D Printed Photosynthetic Wearables Shine New Light on Art, Design, Science & Technology at TED2015*, STRATASYS (May 13, 2015), <http://blog.stratasys.com/2015/05/13/neri-oxman-ted-2015/> [<https://perma.cc/B9BN-Y6F5>].

designs.⁵⁴ This new 3D bioprinting application blurs the boundary between nature and the human body, and contains functional materials that can be tuned for mechanical and optical properties in order to interact with the surrounding environment.⁵⁵ By augmenting living human tissues with additional living elements that make materials, wearable microbiomes can continuously produce useful substances.⁵⁶ The advent of 3D bioprinted wearable microbiomes that nourish skin and repair damaged tissues is challenging the notion of “mother nature” by imparting a living quality into objects.⁵⁷

II. NO BRIGHT-LINE TEST FOR PATENTABLE SUBJECT MATTER IN BIOTECHNOLOGY

3D bioprinting technology is a biotechnological innovation that stresses the U.S. patent regime. As 3D bioprinting matures, patent law will need to respond to a universe where the biological and mechanical worlds will move closer together. Just as other biotechnologies have burgeoned by supporting legal structures, 3D bioprinting presents another biotechnological innovation that will require U.S. patent law to evolve in order to create new products, healthcare solutions, and commerce.

One of the keys to enabling patenting activity in the emerging 3D bioprinting industry will be to not exclude certain inventions from being patent eligible. There has been a rich history of categorical exclusions by courts, resulting in a non-cohesive and inconsistent precedent⁵⁸ on patentable subject matter, and highly subjective interpretations of qualities of inventions being patentable subject matter.⁵⁹

54. Collin Jeffrey, *World's First Photosynthetic Living Matter-Infused 3D-Printed Wearable*, NEW ATLAS (May 18, 2015), <http://newatlas.com/mushtari-3d-printed-photosynthetic-living-embedded-wearable/37548/> [<https://perma.cc/S4TS-J6VQ>].

55. David Sher, *Neri Oxman Takes Us for a 3D Printed Polyjet Ride Into Astrobiological Exploration*, 3D PRINTING INDUSTRY (Nov. 26, 2014), <https://3dprintingindustry.com/news/neri-oxman-polyjet-skin-37099/> [<https://perma.cc/SPY7-5ASX>].

56. *Mediated Matter: Overview*, MIT MEDIA LAB, <https://www.media.mit.edu/research/groups/mediated-matter> [<https://perma.cc/925C-7SXX>] (specifying that wearable microbiomes, which are produced by 3D bioprinting, are embed photosynthetic microbes that convert sunlight into table sugar, which is then consumed by compatible microbes and converted into materials such as scents, colors, pigments, and fuels); see also MIT Media Lab Mediated Matter Group, *Mushtari*, VIMEO (2015), <https://vimeo.com/131786000>.

57. Neri Oxman, *Towards a Material Ecology*, WORLD ECON. F. (Jan. 17, 2016), <https://www.weforum.org/agenda/2016/01/towards-a-material-ecology/> [<https://perma.cc/D9RW-92DL>].

58. Daniel J. Klein, *The Integrity of Section 101: A “New and Useful” Test for Patentable Subject Matter*, 93 J. PAT. & TRADEMARK OFF. SOC’Y 287, 291 (2011).

59. The phrases “patentable subject matter” and “patent eligibility” are synonymous. However, there is a distinction between “patentable subject matter” (being patent eligible) and “patentability,” which refers to whether a patent application fulfills statutory requirements. Thus, “patentable subject matter” (being patent eligible) refers to belonging within a class of inventions for which a U.S. patent

The Federal Circuit has issued decisions that provide guidance on patentable subject matter with biotechnological inventions, but there is no bright-line standard for when an invention derived from a naturally occurring product is considered patentable subject matter.⁶⁰ There has been a history of changes in U.S. patent law as to what biotechnological inventions qualify as patent eligible subject matter.⁶¹ It is unclear as to whether a biotechnological product produced by 3D bioprinting technology would or would not be patentable subject matter.

Regardless of whether one thinks 3D bioprinting inventions *should* or *should not* be patent eligible,⁶² it is universally accepted that the notion

may be sought whereas “patentability” refers to the ability to get a patent application issued after satisfying 35 U.S.C. §§ 101 (utility), 102 (anticipation), 103 (non-obviousness), and 112 (enablement). Thus, if a patent eligible invention is useful, novel, non-obvious, and adequately described in a patent application, then the invention could be patentable if determined so by the USPTO. This means that an invention can be patentable if it first is patent eligible subject matter and if it second also satisfies the requirement in 35 U.S.C. §§ 101, 102, 103, and 112. In other words, patentable subject matter is necessary but not sufficient to warrant patentability. An invention that includes patentable subject matter is only potentially patentable, but whether a patent actually issues still turns on other statutory requirements.

Moreover, a patent attorney or patent agent can inform a client that an invention is “patentable subject matter” (patent eligible) because it qualifies as something for which one could apply for a patent. However, a patent attorney or a patent agent may not inform a client whether an invention is patentable because only the USPTO can make a determination after conducting a search and examination, and assessing responses from the patent attorney or patent agent. Nonetheless, a patent attorney or patent agent may conduct an independent search or provide a written opinion on the patentability of an invention, but it should be noted that such a function is only an opinion, unlike a patentability determination made by the USPTO.

60. The scope of this Article is limited to products, such as 3D bioprinted materials, which are utilized for tissues and organs. This Article does not consider process or method claims specifically, but acknowledges that materials or products produced by 3D bioprinting processes should be evaluated for patentable subject matter. Thus, the Article’s emphasis is on whether 3D bioprinted materials are eligible for or qualify for patent protection, regardless of the process used to produce them. A patentee would be more interested in understanding patenting (or achieving issuance of a patent) of 3D bioprinted end products more so than the processes used to create them; the reason is that a patentee that chose only to pursue a method or a process patent claim could not prohibit a competitor from patenting a different process to arrive at the same 3D bioprinted material. Thus, rather than focus on the minimal protection afforded by process patent claims, this Article presupposes that product patent claims are of more importance to a 3D bioprinting inventor. As a result, the analysis provided herein is centered on 3D bioprinted materials that are captured in a product patent claim, and whether such a drafted patent claim even qualifies as patentable subject matter.

61. The scope of this Article is limited to patentable subject matter for utility patents, which are the majority of all issued U.S. patents. This Article does not consider plant patents, which are governed by 35 U.S.C. § 161 and whose hallmark is “asexual” reproduction of the new plant “variety.” This Article also does not consider design patents, which are governed by 35 U.S.C. § 171 and protect the “new, original and ornamental design for an article of manufacture.” Also, while this Article discusses 3D bioprinted materials that may be utilized for medical applications, it does not delve in-depth into inventions governed by 35 U.S.C. § 287(c), which concerns treatment from medical procedures, is narrowly defined, and provides that there can be no remedy for a patent on certain medical or surgical procedures.

62. This Article does not discuss ethical and moral boundaries raised by advancements in biotechnologies. For an in-depth discussion on whether patents should issue on morally controversial

of patent eligibility *is* of great importance in *affecting* entire industries. Moreover, patentable subject matter is deemed the gateway to patentability, which has more rigorous requirements.⁶³ Therefore, it is critical to understand why, and in what aspects, biotechnological inventions like 3D bioprinting challenge the boundaries of patent eligible subject matter doctrine.

Patent eligibility continues to be an unsettled field. Advents in emerging biotechnologies that seemingly utilize products of nature, such as 3D bioprinting, have posed obstacles to the patent eligibility doctrine. In order to understand the current state of how 3D bioprinting stresses patent eligibility, it is helpful to know how history got us here. Also, identifying any inconsistencies between the USPTO's examination procedures and court decisions on biotechnological inventions regarding products of nature will help clarify the boundaries of patentable subject matter.

A. Overview of 35 U.S.C. § 101

Section 101 of the Patent Act governs which inventions may be patented. According to 35 U.S.C. § 101, "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."⁶⁴ It provides that two criteria for subject matter eligibility must be satisfied: (1) the invention must be directed to one of the four statutory categories (process, machine, manufacture, or composition of matter) and (2) the invention must not encompass a judicially recognized exception.⁶⁵ Patent practitioners draft patent claims⁶⁶ for non-chemical formulation inventions

inventions, such as with the use of embryonic stem cells, genetically modified transgenic animals, and methods of cloning animals, please see Margo A. Bagley, *Patent First, Ask Questions Later: Morality and Biotechnology in Patent Law*, 45 WM. & MARY L. REV. 469 (2003).

63. JANICE M. MUELLER, PATENT LAW 343 (4th ed. 2013).

64. 35 U.S.C. § 101 (2012).

65. U.S. PATENT AND TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2106 I (9th ed. 2015) [hereinafter MPEP] (stating the non-limiting examples of claims that are not directed to one of the statutory categories are: i. transitory forms of signal transmission, ii. a human *per se*, iii. a legal contractual agreement between two parties, iv. a computer program, v. a company, vi. a mere arrangement of printed matter, and vii. data *per se*; further specifying that judicially recognized exceptions include laws of nature, natural phenomena, and abstract ideas).

66. The heart of a patent application or an issue patent is the patent claims, which set forth in worth the metes and bounds of the invention. While legal scholars have debated the analogies between intellectual property conceptualization and real property, in effect, patent claims are akin to a legal description of real estate identified in boundaries of a piece of land.

involving either a process, a product, or an improvement to an existing product or process.⁶⁷

A process is a series of steps that is not excluded as non-statutory subject matter.⁶⁸ In patent practice, a process is commonly termed “methods,”⁶⁹ and is a combination of steps that are manipulative.⁷⁰ Process inventions are typically divided into two types,⁷¹ either “a method of making” or a “method of using.”⁷² For example, in 3D bioprinting, process inventions can involve a treatment of materials,⁷³ or a series of acts⁷⁴ or steps⁷⁵ performed to produce a 3D bioprinted material, such as a method of a 3D bioprinted living tissue or organ. Additionally, a process invention for 3D bioprinting can involve a method of using the 3D bioprinted material in a medical application, such as the earlier application examples of *in vivo* skin repair and a wearable microbiome.

An invention on a product concerns tangible things (objects or artifacts), which in terms of Section 101 consist of machines, manufactures, or compositions of matter. A machine is a concrete thing consisting of parts or devices.⁷⁶ A machine’s novelty lies in its components or the new ways in which the components are combined.⁷⁷ A manufacture is an article produced from raw or prepared materials and is a broadly defined, residual category of manmade items.⁷⁸ Composition of matter includes chemical compounds, mechanical or physical mixtures, and alloys.⁷⁹ For example, tangible 3D bioprinting inventions can include the 3D bioprinter, the material outputted by the 3D bioprinter, the substance

67. See generally John R. Thomas, *Of Text, Technique and the Tangible: Drafting Patent Claims Around Patent Rules*, 17 J. MARSHALL J. COMPUTER & INFO L. 219 (1998).

68. *Ex Parte Murray*, 9 U.S.P.Q.2d 1819 (B.P.A.I. 1988).

69. *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1323 (Fed. Cir. 2009) (explaining that the basic feature for method claims utilizes the preamble in defining the method in terms of the fundamental purpose of the method).

70. JOHN GLADSTONE MILLS ET AL., *PATENT LAW BASICS* § 6:1 (2010).

71. While the distinction in process steps is a matter of characterization, in patent practice there is not much of a substantive effect in such a division.

72. See *In re Pleuddemann*, 910 F.2d 823, 825–26 (Fed. Cir. 1990).

73. *Cochrane v. Deener*, 94 U.S. 780, 788 (1876) (“A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing.”).

74. *NTP, Inc. v. Research in Motion, Ltd.*, 418 F.3d 1282, 1316 (Fed. Cir. 2005) (quoting *Minton v. NASD*, 336 F.3d 1371, 1378 (Fed. Cir. 2005)).

75. *In re Kollar*, 286 F.3d 1326, 1332 (Fed. Cir. 2002) (“A process . . . consists of a series of acts or steps . . . It consists of doing something, and therefore has to be carried out or performed.”).

76. Office of Patent Legal Administration, *Evaluating Subject Matter Eligibility Under 35 U.S.C. § 101: August 2012 Update*, U.S. PATENT AND TRADEMARK OFF. (2012), https://www.uspto.gov/sites/default/files/patents/law/exam/101_training_aug2012.pdf [https://perma.cc/WQ5K-6TM2].

77. MILLS, *supra* note 70, § 6:2.

78. *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980).

79. *Id.*

produced after completion of all of the steps of 3D bioprinting, the chemical formulation (or composition of matter) of the 3D bioprinted material, or the mixture of mechanical and biological components resulting from a 3D bioprinting process. Thus, as discussed in the earlier application examples, 3D bioprinted materials, such as a living tissue for organ transplantation, skin produced for *in vivo* treatment, or a wearable microbiome, may be considered a tangible product in terms of Section 101.

In addition to obtaining inventions on processes and tangible products, inventors can also obtain process patents on newly discovered uses. Under the Patent Act, “a process can include a new use of a known process, machine, manufacture, composition of matter, or method.”⁸⁰ In other words, an inventor can protect a newly discovered property of a known product or newly discovered uses of a known process.⁸¹ For example, as mentioned earlier with 3D bioprinting application examples, a 3D bioprinted invention can protect newly discovered biological properties of 3D bioprinted skin for new cosmetic testing purposes or a 3D bioprinted wearable microbiome for new spacesuit designs. Moreover, a 3D bioprinting invention can protect a newly discovered use of known steps of a 3D printing process, such as utilizing 3D printing processes for *in vivo* skin treatment.

While not mentioned in the Patent Statute, the judicially-created⁸² product-by-process claim is another way to protect inventions, defining the product by its method or process of construction.⁸³ Product-by-process patent claims are an alternative strategy⁸⁴ for capturing the product by how

80. 35 U.S.C. § 100(b) (2012).

81. However, such newly discovered properties or uses would still be subject to the proprietary interests of others and must meet anticipation (or § 102) requirements. The point being made here is not about patentability, but instead that newly discovered properties or newly discovered uses would also be patent eligible subject matter.

82. Mark D. Passler, *Product-By-Process Patent Claims: Majority of Court of Appeals for the Federal Circuit Forgets the Purpose of the Patent Act*, 49 U. MIAMI L. REV. 233, 235–40 (1994) (describing the tortured history of the product-by-process claim where at first, courts recognized the claims by describing the end product by the process of how it was produced, which began with the 1891 case of *Ex Parte Painter* that established the Necessity Rule, whereby product inventions could be protected through process terms when process terms were the most accurate manner in which to describe the invention).

83. MORGAN D. ROSENBERG, *ESSENTIALS OF PATENT CLAIM DRAFTING* (Matthew Bender ed., 2016) (considering a product-by-process claim to be a hybrid of an apparatus claim and a method claim, and as a composition of matter or article manufactured by a particular process; further suggesting that product-by-process claims have long been interpreted only by a product produced by the same process described in the claim, such that a product-by-process claim defines the product itself and not the process and, therefore, an identical product made in a different manner than stated in the claim would not infringe the product-by-process patent claim).

84. Jason R. Strobel, *Product-by-Process Claims: Product or Process Claims?*, HAHN LOESER (June 4, 2009) <http://www.hahnlaw.com/experience/product-by-process-claims-product-or-process-claims-jason-r-strobel-esq> [<https://perma.cc/LH8D-SJ6N>] (suggesting that product-by-process patent

it is made.⁸⁵ While narrower than a composition of matter claim⁸⁶ and a pure product claim,⁸⁷ a product-by-process claim could protect a limited set of 3D bioprinted materials that are described by a specific 3D bioprinting process to make them.

U.S. patent law requires that a patent claim be directed to one of these four patent eligible subject matter categories or be a product-by-process patent claim. Patentable subject matter must fit within judicial limits established by the Supreme Court and the Federal Circuit.⁸⁸ If a patent claim does not fit within one of these categories, then the patent claim will not be patent eligible and would be considered non-statutory subject matter.

B. Products of Nature Are Not Patentable Subject Matter

A U.S. patent protects an invention based on human ingenuity but not on something already existing in nature. The public domain of nature is not patentable subject matter in U.S. patent law because it is for all of humanity to share.⁸⁹ Thus, it is important to draw boundaries to protect the public domain from private property rights.

Nature-based products are not patentable subject matter, even when they are newly discovered and brought to the public attention.⁹⁰ The reason for this is that the patent system is designed to incentivize and reward inventive activity, and the discovery of preexisting items does not involve human-created ingenuity or development. In effect, one who goes into nature and simply brings a product of nature into the public domain does not have a discovery worthy to be a patent.

Assuming this exemption for products of nature does not apply to a certain 3D bioprinting invention, then 3D bioprinting inventions might fit within multiple categories of patentable subject matter. In fact, it may seem that nearly all 3D bioprinted inventions can fit into one of these

claims are most frequently used in chemical and biological technology inventions for protecting products with references to the process steps of its production only when the product cannot be defined in any other way).

85. ROBERT C. FABER, *LANDIS ON MECHANICS OF PATENT CLAIM DRAFTING* §§ 5:2, 10:5 (5th ed. 2008) (defining a product-by-process claim as one where an element of the article is claimed by reciting the process for fabrication of the article or element by using a method claim or method limitations for the process step in which the product or its elements are formed).

86. *Id.* § 6:1 (defining compositions of matter as products where the chemical nature of the substance or material used is the distinguishing feature and utilizes a chemical element or compound).

87. *Id.* § 5:1 (defining an article of manufacture, or a product or apparatus, as a combination of elements such that the elements are tied together in a mechanism or with the use of means-plus-function clauses).

88. Laura Masterson, *The Future of Medical Device Patents: Categorical Exclusion After Ebay, Inc. v. Mercexchange, L.L.C.*, 20 B.U. J. SCI. & TECH. L. 274, 279 (2014).

89. Brief for Respondent at 5, *Bilski v. Kappos*, 561 U. S. 593 (2010).

90. MPEP, *supra* note 65, § 2105 II.A.4.

statutory categories, or the judicially-created product-by-process claim, with some imagination and creativity. In general, the linguistic separation between the statutory categories is nothing more than rhetorical divisions for biotechnological inventions.⁹¹ Because clever patent claims drafting will allow one to capture inventions to fit within one of these categories,⁹² the disconnect between the advent of 3D bioprinting and patent law is not of statutory categorization.

Instead, what is critical for 3D bioprinting inventions is to determine how far patent law can reach in determining what may be patentable subject matter. Because 3D bioprinting increasingly blurs the line between living and nonliving, and potentially between digital and physical worlds, the patent system will need to react by redefining its standard for assessing patentable subject matter. In order to redefine the standard, it helps to understand how courts have assessed patentable subject matter and attempted to define the breadth of what Section 101 allows.

C. *Biotechnology Decisions by the U.S. Supreme Court and Federal Circuit Courts*

What qualifies as patentable subject matter has been a source of considerable debate since the inception of biotechnological applications.⁹³ Early cases concerning products of nature in biotechnology patents focused on biological purification processes to produce compounds. In the 1911 case *Parke-Davis & Co. v. H.K. Mulford Co.*, the patent on purified adrenaline created by structural differences from the natural form derived from animal glands was upheld.⁹⁴ Judge Learned Hand reasoned that because the adrenaline was isolated and purified from its natural surroundings, it was not a product of nature and was a new product both commercially and therapeutically.⁹⁵

Parke-Davis was the foundation of the product-of-nature question in patent law, demonstrating the lack of a clear line between the natural and non-natural in patent law.⁹⁶ Following *Parke-Davis*, in 1931, the Supreme

91. See generally Dan L. Burk, *The Problem of Process in Biotechnology*, 43 HOUS. L. REV. 561 (2006–2007) (suggesting a great deal of trouble exists in distinguishing between product and process inventions in biotechnology, and proposing that a new use of a product is already encompassed in the product patent, even when entitled to a patent on the new process).

92. Tun-Jen Chiang, *Fixing Patent Boundaries*, 108 MICH. L. REV. 523, 537 (2010).

93. ROBERT A. BOHRER, A GUIDE TO BIOTECHNOLOGY LAW AND BUSINESS 77 (2007).

94. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911).

95. Jacob S. Sherkow & Henry T. Greely, *The History of Patenting Genetic Material*, 49 ANN. REV. GENET. 161, 164 (2015).

96. Christopher Beauchamp, *Patenting Nature: A Problem of History*, 16 STAN. TECH. L. REV. 257, 262–63 (2013) (summarizing that before *Parker-Davis*, patents concerning biological substances merely extracted natural sources, and *Parker-Davis* provided a template for hormone patenting, creating a gateway to patenting isolated biological structures).

Court in *American Fruit Growers* held that an orange dipped in a solution of borax to render the skin mold resistant was not a manufactured article and thus was not patentable.⁹⁷ The decision considered whether the addition of a chemical to a product of nature was a new use or property. The Supreme Court held that the addition of borax to a rind of fruit only protects the natural article and does not produce a new article with a “distinctive form, quality, or property.”⁹⁸ Thereafter, in 1938, the U.S. Court of Customs and Patent Appeals held in *In re Merz* that a purified substance that differed from that found in nature is patentable subject matter.⁹⁹

These early cases demonstrated that a product of nature that undergoes a change from its state in nature, whether in encountering a structural difference or being purified, would be patentable subject matter. However, no case precisely defined what constituted a change from nature, or whether purification was required to be a certain amount, degree, or kind. The purification issue was revisited in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, which found that a specific combination of different kinds of bacteria was not patent eligible because the invention covered the aggregation of bacteria, which did not “create a state of inhibition or of non-inhibition in the bacteria” and which was a quality that was “free to all men.”¹⁰⁰

Patents of modified products of nature for biotechnology applications continued to be obtained in the 1950s and 1960s, and without much controversy for decades after.¹⁰¹ Patents with a claim element of “gene” and for “DNA” were issued in the 1970s.¹⁰² However, it remained generally understood that nonliving objects that were not changed from their natural state were not patentable subject matter until the landmark *Diamond v. Chakrabarty* decision.¹⁰³

97. *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1, 11 (1931).

98. *Id.* at 11–12; see also *In re Ewald*, 129 F.2d 340, 342 (C.C.P.A. 1942) (holding that a cored pear was not manufactured because it did not possess a new name, character, or use).

99. *In re Merz*, 97 F.2d 599, 601 (C.C.P.A. 1938) (assessing the outlines of the purification doctrine by determining that while a patent on a method for producing a greater degree of purity than what is produced by a former method is not patentable subject matter, there is an exception if the process produces an article of purity that differs in kind and that may be patentable subject matter).

100. *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127–30 (1948).

101. See *Sherkow & Greely*, *supra* note 95, at 164–65 (summarizing that successful patents were attained for nucleotide derivatives throughout the 1950s and 1960s, including for synthesized nucleotide polyphosphates in 1968, and for RNA and other increasingly complex products of biological intervention).

102. Andrew W. Torrance, *Synthesizing Law for Synthetic Biology*, 11 MINN. J. L., SCI., & TECH. 629, 639 (2015) (specifying that for the first time in 1971, a patent with a claim element of “gene” appeared in U.S. Patent No. 3,710,511, and a patent issued with “DNA” as a claim element in U.S. Patent 3,755,086).

103. See *Diamond v. Chakrabarty*, 447 U.S. 303, 309–10 (1980).

1. The Landmark Chakrabarty Decision

In 1980, the Supreme Court encountered a biotechnology invention that promoted changes from nature with the advent of gene-related innovations. In *Diamond v. Chakrabarty*, the inventor made three types of claims: first, a process claim for the method of producing bacterium; second, claims for an inoculum that comprised a carrier material floating on water, such as straw, and the new bacterium; and third, claims to the bacterium itself.¹⁰⁴

The patent claim directed at the oil-eating bacterium was rejected by the USPTO as not constituting patentable subject matter because bacterium was considered a: 1) product of nature and 2) living thing.¹⁰⁵ However, the Supreme Court rejected these two grounds and found the bacterium to be patentable subject matter because the bacterium was “a nonnaturally occurring manufacture or composition of matter.”¹⁰⁶ The Supreme Court declared that “anything under the sun that is made by man” was eligible for patent protection.¹⁰⁷ The Supreme Court upheld the patent because, unlike the bacterium in *Funk Brothers*, the bacterium was manipulated nature. The Supreme Court widely interpreted the terms “manufacture” and “composition” of matter in reasoning that the patent claim directed to the bacterium was “a product of human ingenuity with a distinctive name, character, and use.”¹⁰⁸ The Supreme Court stated: “Here, by contrast, the patentee has produced a new bacterium with *markedly different characteristics* from any found in nature and one having the potential for significant utility. His discovery is not nature’s handiwork, but his own; accordingly, it is patentable subject matter under §101.”¹⁰⁹

The “markedly different characteristics” language was not the test utilized in *Chakrabarty*.¹¹⁰ Instead, “markedly different characteristics” was an observation in the case that was later adopted as a standard by the Federal Circuit for assessing patentable subject matter of genes in *Association for Molecular Pathology v. Myriad Genetics, Inc.* (hereinafter

104. U.S. Patent No. 4,259,444 (filed June 7, 1972) (specifying a human-made, genetically engineered bacterium capable of breaking down multiple components of crude oil, and discussing that such a property is possessed by no naturally occurring bacteria and is believed to have significant value for the treatment of oil spills).

105. See *Diamond*, 447 U.S. at 309–10.

106. *Id.*

107. *Id.* at 309.

108. *Id.* at 309–10 (quoting *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887)).

109. *Id.* at 310 (emphasis added).

110. Letter from Herbert C. Wamsley, Exec. Director, Intellectual Prop. Owners Ass’n, *Mayo-Myriad* Guidance to USPTO (July 31, 2014), <http://www.ipo.org/wp-content/uploads/2014/08/Myriad.pdf> [<https://perma.cc/DLX4-TVEM>].

Myriad).¹¹¹ The Supreme Court in *Chakrabarty* was not establishing “markedly different characteristics” as a standard and it did not provide additional support for what “markedly different” meant.

The consequence was an expansive approach to patent eligibility with seemingly no patentable subject boundaries, which has spawned significantly more investment in the biotechnology industry.¹¹² The Supreme Court’s reasoning in *Chakrabarty* reiterated that even though the Supreme Court and the Federal Circuit had established the judicial limits on what may be patentable subject matter, not every invention is embraced only within statutory terms.¹¹³ In fact, *Chakrabarty* provided support that the language of Section 101 was meant to be broad and not off-limits, especially because technological advances are not foreseeable.¹¹⁴ The central holding of *Chakrabarty* allowed life forms that encountered human intervention to be a boon to the biotechnology industry.¹¹⁵ *Chakrabarty* reinforced that Congress intended patent laws be given wide scope beyond the time that technologies envisioned when the Patent Act was drafted.¹¹⁶

2. Clarifying Markedly Different in the Myriad Decision

The markedly different characteristics standard was put to test in *Myriad*, which involved a suit filed against Myriad Genetics, seeking to invalidate their claims on isolated DNA on the grounds that the claims covered unpatentable subject matter.¹¹⁷ The plaintiffs challenged that the composition of matter claims that covered isolated DNA had retained the same nucleotide sequence as native DNA and, therefore, were unpatentable as a product of nature.¹¹⁸ The district court judge held the genes were unpatentable because they were not markedly different from

111. Samantak Ghosh, *Gene Patents: Balancing the Myriad Issues Concerning the Patenting of Natural Products*, 27 BERKELEY TECH. L.J. 241, 250 (2012); Ass’n for Molecular Pathology v. Myriad Genetics, Inc., 653 F.3d 1329 (Fed. Cir. 2011).

112. K.K. SINGH, BIOTECHNOLOGY AND INTELLECTUAL PROPERTY RIGHTS: LEGAL AND SOCIAL IMPLICATIONS 31 (2015).

113. See *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

114. *Id.*

115. Rebecca S. Eisenberg, *The Story of Diamond v. Chakrabarty*, in INTELLECTUAL PROPERTY STORIES 256–57 (Jane C. Ginsburg & Rochelle Cooper Dreyfuss eds., 2006); Robert Greene Sterne & Lawrence B. Bugaisky, *The Expansion of Statutory Subject Matter Under the 1952 Patent Act*, 37 AKRON L. REV. 217, 223–23 (2004).

116. See *Diamond*, 447 U.S. at 308.

117. See generally Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F. Supp. 2d 181 (S.D.N.Y. 2010), *aff’d in part, rev’d in part*, 653 F.3d 1334 (Fed. Cir. 2011).

118. *Id.* at 181–84 (discussing the composition of matter claims covering two “isolated” human genes, BRCA1 and BRCA2, which were found to be associated with a predisposition for breast and ovarian cancer).

native DNA; purification alone did not change the essential characteristics of nucleotide sequence of the DNA.¹¹⁹

On appeal, the U.S. Court of Appeals judges had differing opinions. Judge Lourie found that isolated DNA was patentable subject matter and “markedly different” because it was not covalently bonded to other genetic material because it was cleaved from native DNA and synthesized to consist of only a small fraction of a naturally occurring DNA molecule.¹²⁰ Judge Lourie distinguished purification in *Myriad* from that of *Parke-Davis* by clarifying that isolated DNA was not purified DNA because “purification makes pure what was the same material.”¹²¹ In other words, Judge Lourie viewed that a product of nature became “markedly different” through changes in “covalent bonding,” “cleaving,” and “synthesis,” as long as the end result was not the same material.

In the concurring opinion, Judge Moore posited that “markedly different” meant an enlargement of utility or a new utility.¹²² Unlike Judge Lourie, who focused on the change in chemical structure as identifying “markedly different characteristics,” Judge Moore felt that a change in chemical structure was not enough to be considered “markedly different.” Instead, Judge Moore suggested that a product of nature must be used in a different way, which in science happens through exploiting either the properties or the function of a material for a purpose.

By contrast, dissenting Judge Bryson found the gene and gene fragments to be unpatentable subject matter because the structural changes were merely “incidental to the extraction of the genes from nature” that had “no other uses other than their native counterpart.”¹²³ Judge Bryson’s reasoning was that the isolated DNA was not a new use that differed from its native use, but simply a consequence of possession that was similar to extraction of minerals from the earth.¹²⁴ In other words, Judge Bryson viewed that a product of nature could not become “markedly different” unless there was another use separate from possession.

In sum, the differing judges all agreed that a product that was “markedly different” from nature was patentable subject matter. However, they disagreed as to what was considered “markedly different.” Whereas Judge Lourie focused on “markedly different” being a distinctive chemical identity, Judge Moore focused on a new utility and not just a literal chemical difference, and Judge Bryson required comparing both the

119. *Id.* at 231–32.

120. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 653 F.3d 1329, 1351–52 (Fed. Cir. 2011).

121. *Id.*

122. *Id.* at 1364–67.

123. *Id.* at 1375–79.

124. *Id.* at 1375–78.

structure and utility to what was found in nature.¹²⁵ Judge Moore and Judge Bryson both focused on structural differences as a factor in there being “markedly different characteristics,” but neither considered structural differences to be the sole determination of “markedly different characteristics.”

Upon review, the Supreme Court addressed whether a substance isolated from a product of nature constituted patentable subject matter. The Supreme Court held that naturally occurring DNA segments were products of nature and not patentable subject matter simply by being isolated, whereas cDNA was patentable subject matter because it was not naturally occurring.¹²⁶ The Supreme Court reasoned that genes contained in the form of cDNA would be patentable subject matter because cDNA is a synthetic creation by scientists.¹²⁷ In determining that cDNA was patentable subject matter, the Supreme Court articulated that an artificial process of reverse transcribing mRNA *in vitro* was not naturally occurring.¹²⁸ The Supreme Court never stated cDNA satisfied or needed to satisfy “markedly different characteristics” from nature to be patentable subject matter.¹²⁹ While the Supreme Court identified a synthetic product as being non-naturally occurring, its reasoning neither discussed “markedly different characteristics” nor gave a clear standard for determining patentable subject matter.

D. Guidance from the USPTO

The Supreme Court in the *Chakrabarty* and *Myriad* decisions missed a chance to define unpatentable subject matter. The Supreme Court in *Chakrabarty*¹³⁰ addressed that man-made life forms were patentable subject matter and in *Myriad*¹³¹ determined that cDNA as a synthetic creation was patentable subject matter. But the Supreme Court did not define with sufficient detail what constituted “man-made” and “synthetic.” These ill-defined labels were subjective, simplified, and vague. The labels were effectively an “I know when I see it”¹³² test and avoided the underlying analysis of patentable subject matter.

125. *Id.* at 1351, 1367–78.

126. *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2113 (2013).

127. *Id.* at 2119 (reasoning that even though the genes contained in cDNA do occur in nature, cDNA itself does not occur in nature).

128. *Id.* at 2107.

129. *See* Wamsley, *supra* note 110.

130. *See* *Diamond v. Chakrabarty*, 447 U.S. 303, 305 (1980).

131. *See* *Ass’n for Molecular Pathology*, 133 S. Ct. at 2119.

132. *Jacobellis v. Ohio*, 378 U.S. 184, 197 (1964) (considering “I know it when I see it” as a categorical exclusion to the protection of obscenity in the First Amendment).

These cases provided significant uncertainty for lower courts and the USPTO, which responded by initially issuing guidance in March 2014 and June 2014 to assist USPTO examiners with determining what constituted patentable subject matter.¹³³ After practitioners responded with criticism, the USPTO issued a new “Interim Guidance on Patent Subject Matter Eligibility” in December 16, 2014 (hereinafter Interim Guidance) and provided numerous examples applying their guidance to products of nature.¹³⁴

The Interim Guidance provides a bifurcated method for analyzing patentable subject matter for product claims and method claims, with the question of whether a product claim directed to natural phenomena has markedly different characteristics from its origin in nature.¹³⁵ The Interim Guidance instructs USPTO examiners to apply their broadest reasonable interpretation¹³⁶ in applying the Supreme Court’s reasoning as follows:

1. Step 1: “Is the claim to a process, machine, manufacture, or composition of matter?” *If yes, then go to Step 2. If no, then claim is not patentable subject matter.*
2. Step 2A: “Is the claim directed to a law of nature, a natural phenomenon, or an abstract idea (judicially recognized exceptions)?” *If no, the claim is eligible as patentable subject matter, and the claim should be examined for patentability. If yes, go to Step 2B.*
3. Step 2B: “Does the claim recite additional elements that amount to significantly more than the judicial exception?” *If yes, the claim is eligible for patent protection and should be patentable subject matter. If no, then claim is not eligible as patentable subject matter.*¹³⁷

The Interim Guidance reiterates under Step 1 that a claim is eligible under 35 U.S.C § 101 as long as the claim is directed to one of the four statutory categories of process, machine, manufacture, and composition of

133. Cong Yao et al., *Patent Eligibility of Nature-Based Products: Current View of the United States Patent & Trademark Office*, 11 INDUS. BIOTECH. 91, 91 (2015), <https://www.fr.com/wp-content/uploads/2014/10/230826.pdf> [<https://perma.cc/DH9G-WMW6>].

134. U.S. PATENT & TRADEMARK OFFICE, 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY 79 FR 74618-01 (2014), <http://federalregister.gov/a/2014-29414> [<https://perma.cc/2DRB-4PFB>].

135. Roy P. Isaac et al., *Analysis of USPTO’s 2014 Interim Guidance on Patent Subject Matter Eligibility: Impact on Hightech Biotech Industries*, AM. INTELL. PROP. L. ASS’N (Jan. 2015), http://www.aipla.org/committees/committee_pages/Biotechnology/HT/Shared%20Documents/HT_Buzz_201501.pdf [<https://perma.cc/B2Z2-VKZE>].

136. MPEP, *supra* note 65, § 2111 (stating that during patent examination, the pending claims must be “given their broadest reasonable interpretation consistent with the specification”).

137. *See* Yao et al., *supra* note 133, at 91.

matter.¹³⁸ Most product claims should easily satisfy the first step in the Interim Guidance analysis.

For products claims that are directed to natural phenomena, Step 2A considers whether the claimed subject has markedly different characteristics from its counterpart in nature based on the product's structure, function, and/or properties.¹³⁹ The conceptualization of what can be "markedly different characteristics" is broader in the Interim Guidance than in the original March 2014 and June 2014 Guidelines, which limited "markedly different characteristics" to only structural changes and excluded functional changes from products of nature.¹⁴⁰ The Interim Guidance's Step 2A declares a nature-based product that is not directed to a judicial exception because it is markedly different would be patentable subject matter.¹⁴¹

The Interim Guidance's statement that "even small change can result in markedly different characteristics"¹⁴² seems to suggest a lenient standard in covering nature-based products.¹⁴³ Since USPTO patent examiners must apply the broadest reasonable interpretation allowed by the USPTO, then Step 2A seems to suggest a broad framework where biotechnological discoveries aided by man and not simple repetitions from nature could be patentable subject matter.¹⁴⁴ The USPTO Interim Guidance provides non-limiting examples that qualify as being "markedly different," including: biological or pharmacological functions, chemical and physical properties, phenotype, including the functional and structural characteristics of an organism, and structure and form.¹⁴⁵

Under the Interim Guidance Step 2A, if a patent claim is indeed directed to a judicial exception because it not "markedly different," then the USPTO examiner is required to analyze whether the claimed matter is "significantly more" than the judicial exception.¹⁴⁶ The Interim Guidance

138. Ryan M. Corbett, *USPTO Issues Patent Eligibility Guidelines... So Now What?*, INSIDE COUNSEL (Mar. 11, 2015), <http://www.insidecounsel.com/2015/03/11/uspto-issues-patent-eligibility-guidelines-so-now> [<https://perma.cc/D9D3-UXM4>].

139. See Isaac, *supra* note 135.

140. See Yao et al., *supra* note 133, at 91.

141. *Id.* at 91–93.

142. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

143. See generally Yao et al., *supra* note 133.

144. *Id.*

145. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134, at 10 (further defining the markedly different examples as follows: a biological or pharmacological function or activity could be a bacterium's ability to infect leguminous plants or the protein-encoding information of a nucleic acid; chemical or physical properties could be the alkalinity of a chemical compound, or the ductility or malleability of metals; a phenotype's functional or structural characteristics could be the shape, size, color, and behavior of an organism; and structure and form could be the physical presence of plasmids in a bacterial cell or the crystalline form of a chemical).

146. *Id.*

give numerous factors that appear to depend on the claim language and specific facts of the technology.¹⁴⁷ While some commentators suggest that differential structure features would garner a technology to be patentable subject matter, the inherent vagueness of what could be “significantly more” is not conclusive. Examination under Step 2B is simply ill-defined.

Thus, it appears that a product of nature with a patent claim encompassing a structure, function, or property different than that found in nature would be considered patentable subject matter. However, the Interim Guidance does not give a clear standard on what constitutes a changed structure, function, or property.¹⁴⁸ While examples are provided, no bright-line test appears to delineate the boundaries of a structure, function, or property. Moreover, the Interim Guidance forecloses something other than a change in structure, function, or property can achieve a “markedly different characteristic” than that found in nature.¹⁴⁹

In addition, the Interim Guidance does not mention whether any changes to a human organism would be considered markedly different in structure, function, and/or property.¹⁵⁰ The Interim Guidance assumes that products of nature are biological but does not consider any limitations to nature, such as whether human organisms are prohibited from consideration. For example, a product of nature in human form that undergoes a markedly different change could conceivably be patentable subject matter under the Interim Guidance. Another avenue for patenting a nature-based product of human form would be to fulfill the requirements in the American Invents Act. In other words, the lack of reference to humans in the Interim Guidance does not eliminate patentable subject matter requirements found elsewhere. The next Section evaluates how patentable subject matter of nature-based products must still pass the requirements in the AIA, and Part III analyzes both the requirements of the Interim Guidance and the AIA with the advent of 3D bioprinting.

147. See Isaac et al., *supra* note 135, at 92 (summarizing that factors supporting patentable subject matter include improvements to another technology, improvements to functioning of a machine, effecting a transformation or reduction of a particular article to a different state or thing, adding a specific limitation other than what is well-understood, or adding unconventional steps; further summarizing that factors that cut against patentable subject matter include mere inclusion of instructions to implement an abstract idea on a computer, appending well-understood activities previously known to the industry, appending insignificant extra-solution activity, or mere data gathering in conjunction with a law of nature or abstract idea).

148. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

149. *Id.*

150. *Id.*

E. *America Invents Act's Silent Amendment with Undefined Human Organism*

The Supreme Court opinions in *Chakrabarty* and *Myriad* fell short on prescribing a bright-line test for the patent eligibility of biotechnology inventions.¹⁵¹ The USPTO Interim Guidance centers on nature-based products and does not consider how to evaluate human organisms.¹⁵² By not considering human organisms in relation to nature-based products that undergo markedly different changes, the Interim Guidance presupposes that AIA's reference to human organisms is an exception to patentable subject matter.

Section 33 of the AIA states "notwithstanding any other provision of law, no patent may issue on a claim directed to or encompassing a human organism."¹⁵³ However, the words "directed to," "encompassing," and "human organism" in Section 33 are undefined. While the words "directed to" and "encompassing" are well known terms of patent practice, the phrase "human organism" can be construed broadly.¹⁵⁴ Because "human organism" is undefined in the AIA, the USPTO and the courts lack the information necessary to determine the correct scope of patents claiming aspects of human organisms. While the AIA attempts to redefine how a "human organism" is patentable subject matter, it will likely be left to the courts to decide what the law means.

In effect, the AIA's lack of definition of the phrase "human organism" serves as a silent amendment by Congress to restrict the patentable subject matter doctrine. The AIA serves as public law that prohibits any form of "human organism" from being patentable subject matter without an explicit definition. As a *sub silentio* reference to patentable subject matter, the AIA serves as an implicit amendment to what inventions can be patented under Section 101. Said another way, "human organism" and "markedly different" are considered two separate evaluation criterion that must both be satisfied under patentable subject matter doctrine.

151. See *supra* notes 78, 117, 120 and accompanying text.

152. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134 and accompanying text.

153. Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (codified as amended in scattered sections of 35 U.S.C.).

154. This Section briefly investigates "directed to" and "encompassing" because each is commonly used and not considered vague in patent law practice. The analysis of "directed to" and "encompassing" is tied to its interaction with the term "human organism," which can have varying definitions in technology and patent law. A central claim of this Article is that the phrase "human organism" will need to be better defined in light of the advent of 3D bioprinting, which will require patent law to evolve as advances in 3D bioprinting technology and novel applications will create tensions with existing patent law.

In reviewing Section 33, the relevant question as it relates to the scope of this Article in Part III is whether 3D bioprinting and its outputs can be excluded as patentable subject matter.¹⁵⁵ Such a determination cannot be made by a rote application of Section 33's language, but also includes statutory construction, legislative history, and congressional intent.

1. Statutory Construction of "Human Organism"

While statutory interpretation as a tool can help us understand the meaning of a statute, there are a multitude of techniques and a host of problems that arise with any approach to interpretation. Statutory interpretation includes strict constructionist, textualist, or purposivist approaches.¹⁵⁶ A strict constructionist approach uses canons and rules of interpretation to establish the meaning of the words in the statute; this literal approach takes a statute in its ordinary literal and plain meaning.¹⁵⁷ A textualist approach interprets words in the context apparent to a reasonable person and in the context of the underlying purpose of the statute. Textualists give the actual words respect, rather than sticking religiously to interpreting them; they do not consider legislators' psychological intentions and expectations.¹⁵⁸ The purposivist approach focuses on the purposes of the statute, which suggests that the legislature is made up of "reasonable persons pursuing reasonable purposes reasonably."¹⁵⁹

Each of these approaches to statutory interpretation can be used to interpret the meaning of Section 33 of the AIA. However, because "directed to," "encompassing," and "human organism," are not defined in the AIA, the interpretations will inherently yield differing results. A lack

155. Leahy-Smith America Invents Act § 33.

156. Richard H. Fallon, Jr., *The Meaning of Legal "Meaning" and Its Implications for Theories of Legal Interpretation*, 82 U. CHI. L. REV. 1235, 1243–44, 1269 (2015) (inquiring about the definition of "meaning" and suggesting that theories regarding the meaning of legal provisions share concerns about communicative content; further delineating that literalists (or strict constructionists) discern meaning solely from dictionary definitions, the rules of grammar, or the meaning of a sentence emerging from a combination of elements, textualists embrace context-dependent meanings, and purposivists seek to understand the product of reasonable legislators seeking to pick out reasonable meaning).

157. See Fallon, *supra* note 156.

158. Richard H. Fallon, Jr., *Three Symmetries Between Textualist and Purposivist Theories of Statutory Interpretation—And The Irreducible Roles of Values and Judgment Within Both*, 99 CORNELL L. REV. 685, 685–87, 707–09 (2014) (discussing that textualists emphasize a statute's "semantic context," seek to understand how a reasonable person would understand statutory language in context, and hold that judges should strive to exclude their own values from the interpretive process); Cory R. Liu, *Textualism and the Presumption of Reasonable Drafting*, 38 HARV. J.L. & PUB. POL'Y 711 (2015).

159. Victoria Nourse, *Misunderstanding Congress: Statutory Interpretation, the Supermajoritarian Difficulty, and the Separation of Powers*, 99 GEO. L.J. 1119, 1147–48 (2011).

of defined terms is particularly problematic because a broad range of inventions treating humans could be invalidated, and contentious future litigation depends on the interpretation of these words.

First, the phrase “directed to” under the strict constructionist approach would yield a dictionary definition of “to go in a desired direction; aim,” and under a textualist approach in the context of its appearance in the AIA, would mean “to control or conduct the affairs of.”¹⁶⁰ Second, the phrase “encompassing” under the strict constructionist approach would yield a dictionary definition of “including (something) as a part.”¹⁶¹

Additionally, under the purposivist approach, the AIA’s terms “directed to” and “encompassing” could be interpreted differently in patent practice vernacular. Because reasonable patent practitioners sometimes use the phrase “directed to” to indicate the core of a claimed invention, then “directed to . . . a human organism” could permit patenting of a human being per se. Similarly, because the word “encompassing” is sometimes used by patent practitioners as an open transition defining phrase (such as “comprising” or “including”) to define a specific patent claim’s elements, then “encompassing a human organism” could mean that humans could be an element of an invention. Thus, the purposivist approach in patent practice vernacular suggests broad interpretations of “directed to” or “encompassing” humans; this leaves open a possibility that a judge could construe either “directed to” or “encompassing” differently, further confusing the matter.

Third, the phrase “human organism” is the most confounding aspect of Section 33 of the AIA, which leaves the phrase undefined. Moreover, the entire phrase “human organism” is undefined in most dictionaries,¹⁶² although both of the words “human” and “organism” can have varying definitions.¹⁶³ Thus, the strict constructionist approach and the textualist approach would yield differing results. However, the purposivist approach, which centers on the purpose of the statute, could give some guidance through an understanding of the legislative history, described directly below.

160. Ava Caffarini, *Directed To or Encompassing a Human Organism: How Section 33 of the America Invents Act May Threaten the Future of Biotechnology*, 12 J. MARSHALL REV. INTELL. PROP. L. 768, 779 (2013).

161. MERRIAM-WEBSTER’S COLLEGIATE DICTIONARY (11th ed. 2003).

162. *Id.*

163. See Caffarini, *supra* note 160, at 781 (defining a possible definition of “human” as being “of, pertaining to, or characteristic of humankind or people” and “organism” as being “any living entity that contains one or more cells”).

2. Legislative History of Human Organism

As a general rule of statutory construction, a statute is construed to give effect to both the language of the statute and the intent of the legislature, with the language carrying more weight.¹⁶⁴ Even though the starting point of statutory interpretation is the language itself, absent a clearly expressed legislative intention to the contrary, at the very least legislative history can answer the general question of why Congress is making a particular law.

The USPTO and courts can use legislative authority for assessing whether 3D bioprinted material is patentable subject matter because legislative history can guide the interpretation of a statute.¹⁶⁵ Legislative history of the AIA supports there being varying perspectives regarding “human organisms” as patentable subject matter. However, the legislative history of Section 33 has been riddled with contradictions, ad-hoc exceptions, and a lack of coherent guiding principles.¹⁶⁶ The term “human organism” is not defined, seemingly left open for the USPTO and for the courts to determine.

The sponsors of the AIA had utilized a prior legislative act, known as the “Weldon Amendment” of the Consolidated Appropriations Act, that became codified in Section 33.¹⁶⁷ But even the Weldon Amendment does not contain a definition of “human organism,” and its legislative history contains internal contradictions. The Weldon Amendment and remarks made by Representative Lamar Smith in the legislative history of the AIA each specify:

Nothing in this section should be construed to limit the ability of the USPTO to issue a patent containing claims directed to or encompassing:

1. any chemical compound or composition, whether obtained from animals or human beings or *produced synthetically*, and whether identical to or distinct from a chemical structure as found in an animal or human being, including but not limited to nucleic acids, polypeptides, proteins, antibodies, and hormones;
2. cells, tissue, organs or other bodily components *produced through human intervention*, whether obtained from animals, human beings, or other sources; including but not limited to stem

164. Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 971 (Fed. Cir. 2002).

165. Deluxe Corp. v. United States, 885 F.2d 848, 850 (Fed. Cir. 1989) (“[W]here the text itself does not clearly exclude alternate interpretations, we look first to the legislative history for illumination of the intent of Congress.”).

166. Yaniv Heled, *On Patenting Human Organisms or How the Abortion Wars Feed into the Ownership Fallacy*, 36 CARDOZO L. REV. 241, 244 (2014).

167. *Id.* at 256.

cells, stem cells derived tissues, stem cell lines, and viable synthetic organs;

3. methods for creating, modifying, or *treating human organisms*, including but not limited to methods for creating embryos through in vitro fertilization, methods of somatic cell nuclear transfer, medical or genetic therapies, methods for enhancing fertility, and methods for implanting embryos;

4. a *nonhuman organism incorporating one or more genes* taken from a human organism, including but not limited to a transgenic plant or animal, or animal models used for scientific research.¹⁶⁸

Even though such legislative history provides a negative limitation on what may be permitted as patentable subject matter, it does not clarify what may be the boundary of patentable subject matter. Because the legislative history does not delve into what may not be patentable subject matter, inventors do not have guidance when technologies enable inventions that are not specified in a category. The negative limitations specify the phrases “*produced synthetically*,” “*produced through human intervention*,” “*treating human organisms*,” and “*nonhuman organism*,” but do not describe the boundary limits of each phrase. Each of these phrases can extend beyond the scientific understanding of the current definition of the phrase with the advent of a new technology. For example, the advent of 3D bioprinting redefines what some of these phrases mean or provides new examples that were not envisioned previously. This is investigated further in Part III.

This Part suggested that the AIA contains no explanation or definition of what “human organism” means, nor how to apply the law. Without clarity on what “human organism” means in patent law, there is a lack of guidance for the USPTO and the courts. While the AIA attempts to redefine how a human organism is patentable subject matter, it will likely be left to the courts to decide what the law means. Part III evaluates “human organism” in the context of 3D bioprinting and suggests that the advent of 3D bioprinting complicates what a human organism may be and introduces new capabilities to transform some aspect of a human organism. The legislative history of the AIA has not considered emerging technologies such as 3D bioprinting, and its unclear definitions are further obfuscated with new applications that are just being imagined by inventors.

168. 157 CONG. REC. E1182–85 (daily ed. June 23, 2011) (statement of Representative Lamar Smith) (emphasis added).

III. APPLICATION OF PATENTABLE SUBJECT MATTER REQUIREMENT TO 3D BIOPRINTING

The ability to produce living human cells with 3D bioprinting pressures the patent regime. The line between living and nonliving is effectively eroding with 3D bioprinting. This Part confronts this situation directly by investigating 3D bioprinting applications that raise uncertainty with patentable subject matter in light of: 1) the unclear “markedly different characteristics” standard set by courts and the USPTO,¹⁶⁹ and 2) the unclear reference to “human organism” in the AIA and its legislative history.¹⁷⁰

This Part also considers the interplay between the human organism exception and the markedly different characteristics standard in the realm of 3D bioprinting. It investigates 3D bioprinting technology’s ability to challenge patentable subject matter doctrine in ways not imagined by other technologies. First, this Part considers the case of a human organism element input into a 3D bioprinting operation that creates a modified output lacking the human organism element. Second, and perhaps more importantly, this Part considers 3D bioprinting applications where a 3D bioprinted material contains markedly different characteristics than that found in nature, but may still be considered human and therefore not qualify as patentable subject matter under the AIA.

3D bioprinting, like biotechnology in general, can modify products of nature. Unlike other biotechnologies, however, 3D bioprinting processes can co-mingle living and nonliving worlds, either during the 3D bioprinting process or later in integrating 3D bioprinted materials into the human body. Even if 3D bioprinted tissues and organs are not viewed as products of nature, they may still be considered human. This Part investigates the continuum of what may be considered human in light of 3D bioprinting. It analyzes patentable subject matter by examining: What does a human organism mean under patent law for 3D bioprinting? Where does the boundary of a human organism stop and the boundary of the nonhuman organism world begin? What is considered a human organism where products of nature are mixed with artificial, nonhuman organism elements?

169. See *supra* notes 104–147 and accompanying text (explaining the historical and current status of the standard for determining patentable subject matter in the context of biotechnological inventions).

170. See *supra* notes 153–168 and accompanying text (explaining the statutory and legislative history of the AIA in the context of human organism concerning patentable subject matter).

A. *3D Bioprinting Applications Magnify the Human Organism Ambiguity*

3D bioprinting illustrates the problems created by leaving the phrase “human organism” open to judicial construction. The technological capabilities of 3D bioprinting can be assessed to identify how, if at all, “human organisms” applies or further magnifies the deficiencies, ambiguities, and inconsistencies within the legislative history of the Weldon Amendment and Section 33 of the AIA.

First, can 3D bioprinting be considered to fall within *produced synthetically*? Presumably, this part of the Weldon Amendment¹⁷¹ means “by chemical synthesis” because the accompanying text specifies a chemical compound or composition. In the realm of biological applications, synthesis could either be by chemical synthesis or synthetic biology, which refers to the design and fabrication of biological components that do not exist in the natural world, or the redesign of existing biological systems.¹⁷² Thus far, synthetic biology has imported engineering principles into traditional biological sciences and attempted to remake living systems at the molecular level.¹⁷³ While 3D bioprinting technology does enable synthesizing biological components, it does not build living material at the molecular level; instead it builds living material at the cellular level, resulting in aggregation of tissues and organs.¹⁷⁴ On the other hand, synthetic biology’s definitions and applications are based on genetic engineering, genetic programming, and biological engineering.¹⁷⁵ Because the first statement of the Weldon Amendment¹⁷⁶ does not account for cellular production, the drafters did not consider 3D bioprinting technology in exempting synthetic production of anything human. However, other statements in the Weldon Amendment¹⁷⁷ could encompass 3D bioprinting, even though it is not stated.

Second, is 3D bioprinting considered made by *human intervention*? Generally speaking, any type of 3D printer would be considered made by human intervention and operated by human intervention through a click of a button or by computer control; therefore, 3D bioprinting, as a subset of 3D printing, would be considered a human intervention operation.

171. See *supra* notes 166–168 and accompanying text.

172. *What Is Synthetic Biology?*, SYNTHETIC BIOLOGY, <http://syntheticbiology.org/FAQ.html> [<https://perma.cc/434U-GRCU>].

173. See Torrance, *supra* note 102.

174. Christian Mandrycky et al., *3D Bioprinting for Engineering Complex Tissues*, 34 BIOTECH. ADVANCES 422, 422–34 (2016).

175. See Torrance, *supra* note 102.

176. See *supra* notes 166–168 and accompanying text.

177. *Id.*

However, other facets of the 3D bioprinting systems, such as Bio-CAD¹⁷⁸ files, can arguably function without human intervention once created. This is problematic because Bio-CAD files are digital blueprint instructions to print objects and are essentially representative of the objects themselves.¹⁷⁹ Patentees can attempt to capture the eventual 3D bioprinted object in a patent claim encompassing the digital instructions of the 3D bioprinted object.¹⁸⁰ Some Bio-CAD files may be created in an automated fashion by computer control that transposes medical images into a virtual image on a computer.¹⁸¹ Because some Bio-CAD may not require human intervention, patent claims that capture the files as representative blueprint instructions of the biological product or biomaterial to be 3D bioprinted may not be patentable subject matter for effectively being a human organism under this aspect of the Weldon Amendment.¹⁸²

Third, can 3D bioprinting be considered a method for *treating human organisms*? While 3D bioprinting can provide healthcare benefits to treat human organisms,¹⁸³ not all 3D bioprinted materials have a medicinal effect on patients. 3D bioprinted devices such as customized replacement body parts, tailor-fabricated organs, and 3D bioprinting enabled *in situ* skin repair would provide treatment to humans, but other 3D bioprinting applications, such as emerging wearable microbiomes, typically are not

178. See Sun et al., *supra* note 32.

179. See Osborn, *supra* note 19, at 1328 (discussing that as a technological matter, there is little difference between digital files and tangible objects with 3D printing because the digital file and physical printed item can be viewed as interchangeable).

180. See Brean, *supra* note 2.

181. See *generally Biomedical Modeling Inc.: Biocad*, DASSAULT SYSTEMS: SOLIDWORKS, <http://www.solidworks.com/sw/products/details.htm?productID=529> [https://perma.cc/TJG2-QVKY].

182. See *supra* notes 166–168 and accompanying text.

183. It should be noted that in U.S. patent law, 35 U.S.C. § 287(c) creates a liability exception for medical practitioners infringing medical treatment method patents while performing a medical activity with the goal of treating a human being. See 35 U.S.C. § 287(c) (2011). This means that a medical practitioner who infringes a medical treatment method patent is immune from liability to the patentee for any infringement of the patent during the performance of the medical treatment activity. Essentially, 35 U.S.C. § 287(c) deprives a patentee of its infringement remedies (such as a civil trial, injunction, damages, and attorney's fees) where a medical practitioner or a related healthcare entity (such as a hospital, health maintenance organization, or nursing home) performs a patented medical activity.

Therefore, the doctors and healthcare entities who utilize 3D bioprinting inventions for treatment would be immunized from liability for infringement of the 3D bioprinting medical treatment method patents. However, what may be considered “treatment” with the use of 3D bioprinting inventions is unclear. Since other statutory categories of machine, manufacture, or composition of matter may be patented, the medical activity utilizing those types of inventions would not be immunized from patent infringement claims. Thus, courts will need to clarify what kinds of 3D bioprinting inventions and their uses for medical treatment would constitute “medical activity” under the statute. Presumably, insofar as 3D bioprinting digital design files and 3D bioprinted materials are not medical or surgical procedures, then 35 U.S.C. § 287(c) should not cover the patents drawn to such inventions.

being considered treatment and instead are being considered for fashion or spacesuit design.¹⁸⁴ The list of permitted treatment categories in the Weldon Amendment¹⁸⁵ is limited and ignores cases where human organisms are involved, but not necessarily for treatment.

Fourth, the Weldon Amendment¹⁸⁶ ignores technologies lacking utilization of a *nonhuman organism incorporating one or more genes*. The Weldon Amendment was written with the intention of limiting stem cell usage,¹⁸⁷ but was not aimed to suppress genetic engineering development. It focuses on permitting genetic engineering from animal or plant sources and ignores 3D bioprinting, which does not incorporate genetics and instead functions at a cellular level. Moreover, by defining “nonhuman” in attempting to define what may or may not be human, the Weldon Amendment and the legislative history of the AIA conflates what legislators consider a definition of human.

In sum, the Weldon Amendment¹⁸⁸ and legislative history of the AIA do not effectively address what is human and what is nonhuman. The question of what may or may not be considered a human for the purposes of Section 33’s legislative history is ambiguous. This analysis shows that the legislative history of the AIA did not consider the advent of 3D bioprinting. Thus, the lack of clear legislative guidance on patentability further demonstrates that the law must adapt to the challenges offered by emerging technologies such as 3D bioprinting. Alternatively, and as supported by some commentators, without interpreting legislative history, the meaning of Section 33 will either need to be found elsewhere or be based on guidance by federal courts.¹⁸⁹ This is problematic in U.S. patent law, which requires clarity in administering patent examination by the USPTO. Ultimately, unless there is further legislative action, inventors will need to wait until federal courts define how some portion of “human organism” is captured in a patent claim.

B. Bio-CAD Files May or May Not Be Patentable Subject Matter

As mentioned, Bio-CAD¹⁹⁰ files are a digital representation of a human organism or a body part of a human organism. Bio-CAD¹⁹¹ files

184. See *supra* notes 38–57 and accompanying text.

185. See *supra* note 168 and accompanying text.

186. See *supra* notes 166–168 and accompanying text.

187. See Heled, *supra* note 166.

188. See *supra* notes 166–168 and accompanying text.

189. Andrew W. Torrance, *The Unpatentable Human Being*, 43 HASTINGS CTR. REP. 10 (2013).

190. See Sun et al., *supra* note 32.

191. *Biomedical Modeling Inc.: BioCad*, *supra* note 181 (displaying medical imaging data in the form of CT or MRI scans that are utilized to create models of human anatomy for eventual 3D bioprinting); *BioCAD*, BIOMEDICAL MODELING, INC., <http://www.biomodel.com/biocad.html>

cover the information content of a medical image transposed into a virtual object on a computer. Just like 3D printing CAD files contain digital models of non-natural objects, Bio-CAD files contain digital models¹⁹² of a natural or biological object.¹⁹³ Bio-CAD files, like any 3D printing CAD file, contain digital blueprint instructions for an object in the form of a digital 3D model.¹⁹⁴ Medical images of a biological tissue or organ in an MRI or CT scan can be transformed into CAD files as 3D bioprinting ready files.¹⁹⁵

[<https://perma.cc/ST96-UFNP>] (2017) (showcasing that CT and MRI data can be reconstructed into accurate anatomical representations, which is the information content instruction to a 3D bioprinter).

192. This Article does not investigate whether Bio-CAD files could be copyrighted to protect some digital aspects of 3D bioprinting technologies. For a discussion on how 3D printing (or 3D bioprinting, which is a subset of 3D printing) fits within U.S. copyright law, see Peter S. Menell & Ryan G. Vacca, *3D Printing and U.S. Copyright Law* (UC Berkeley Public Law Research Paper No. 2859737), <https://ssrn.com/abstract=2859737> [<https://perma.cc/3JBR-W57E>] (discussing that CAD files or physical objects generally would qualify for copyright protection, but there could be three main reasons for copyright law's exclusion of protection of CAD files: 1) The functional aspects of works of authorship erects a significant barrier to copyrightability of CAD files and three-dimensional objects; 2) The difficulty in separating form from function poses a problem, since many 3D printing designs combine aesthetic and functional features; and 3) Owners of the CAD file would face legal and practical challenges enforcing its copyright, particularly in how to target copyright infringement among Internet Service Providers and software application vendors). For a discussion on doctrinal copyright law issues with 3D printing technology that are related to originality, useful articles, and the functionality doctrine, see Lucas S. Osborn, *Of PhDs, Pirates, and the Public: Three-Dimensional Printing Technology and the Arts*, 1 TEX. A&M L. REV. 811 (2014).

193. Given that the U.S. Copyright Office has rejected copyright registration for genetically engineered DNA sequences, a proposed copyright on Bio-CAD files may not achieve registration with the U.S. Copyright Office. In addition to the challenges for copyrightability identified in *supra* note 192 and *infra* note 198, there are biological-specific challenges to copyright protection. See Christopher M. Holman et al., *Are Engineered Sequences Copyrightable?: The U.S. Copyright Office Addresses a Matter of First Impression*, 35 BIOTECH. L. REP. 103, 104–08 (2016) (discussing the analogy between engineered genetic code and computer code, and suggesting that Congress should amend the Copyright Act to explicitly identify genetic code as a category of copyrightable subject matter; further suggesting genetic code would unlikely be copyrightable in the near term, especially in light of the U.S. Copyright Office's rejection of a synthetic DNA sequence by DNA 2.0, a leading gene synthesis and design company).

194. Sklyer R. Peacock, *Why Manufacturing Matters: 3D Printing, Computer-Aided Designs, and the Rise of End-User Patent Infringement*, 55 WM & MARY L. REV. 1933, 1937 (2014).

195. See Michael P. Chae et al., *Emerging Applications of Bedside 3D Printing in Plastic Surgery*, FRONTIERS IN SURGERY, June 16, 2015, at 1, 4–5 (providing that 3D modeling software can translate a CT/MRI scan into a CAD file, and 3D slicing software can divide the CAD files into thin data sets suitable for 3D printing); Michael W. Itagaki, *Using 3D Printed Models for Planning and Guidance During Endovascular Intervention: A Technical Advance*, 21 DIAGNOSTIC AND INTERVENTIONAL RADIOLOGY 338 (2015) (demonstrating the use of data from a patient's CT scan and free open-source software, to develop a CAD file of a patient-specific, hollow, and small-caliber vascular model treatment of a difficult and unconventional aneurysm while preserving splenic function); Wuyang Shui et al., *The Production of Digital and Printed Resources from Multiple Modalities Using Visualization and Three-Dimensional Printing Techniques*, 12 INT'L J. OF COMPUTER ASSISTED RADIOLOGY AND SURGERY 13 (2016) (validating that neuroimaging technologies such as CT, CTA, MRI, and TOF-MRA of medical images can be transformed into CAD files, which can undergo volume rendering and medical image reconstruction, before being 3D printed).

However, until a Bio-CAD has been modified by human or computer interaction, the Bio-CAD file is a static and visual representation of a biological object that is a click of the mouse away from being 3D bioprinted after it is created. Thus, an unmodified Bio-CAD file of a human organism is information content of a human organism in a digital, pixel representation that can be 3D bioprinted with *de minimis* effort. The line between digital and tangible in 3D printing, as well as in 3D bioprinting, is undefined, and CAD files, such as Bio-CAD files, can be considered as representing the object itself.¹⁹⁶ Would a Bio-CAD file be tantamount to a human organism itself under a vague, markedly different characteristics standard and undefined human organism exception?

Since a CAD file, such as a Bio-CAD file, is simply information in the form of a data package that describes the properties of the object,¹⁹⁷ then it could arguably represent the human organism or a body part of the human organism itself in digital form.¹⁹⁸ This feature could disqualify a

196. See Osborn, *supra* note 19, at 1331 (specifying that a CAD file can be created from scratch using a computer program or by scanning an object, and under either scenario, the CAD file is a digital representation of the physical object that is printed).

197. See Peacock, *supra* note 194, at 1948–51 (describing that the information in a CAD file is best understood as a collection of facts and may either be protected by copyright law or by patent law, depending on how the schematics in CAD files are defined).

198. This Article focuses on patent law, particularly on patentable subject matter. There may or may not be copyright protection for Bio-CAD files, but the law is unclear in that aspect and that topic is beyond the scope of this Article. However, because digital technology in the form of Bio-CAD files is discussed in this Article, for completeness, a brief discussion of the applicability of U.S. copyright law is provided here.

It should be noted that U.S. copyright law considers computer programs to be literary works under the Copyright Act in 17 U.S.C. § 10. U.S. copyright law holds that a copyright attaches only to an original work, which is created when it is fixed in a tangible medium of expression for the first time. Thus, source code to the extent that it reflects the original expression is copyrightable, whereas object code (especially when stored on ROM) is regarded as being part of a machine and is not protectable by copyright. Source code refers to the code actually written by the author in a particular programming language, whereas object code is the code generally translated from the original programming language and compiled by a computer into a machine-readable representation (defined as a string of zeros and ones that are interpretable by a computer). However, object code has been held to be copyrightable by the Ninth Circuit when the computer program, when written, embodies expression (in other words, a computer program that is written in object code and reflective of the original expression is copyrightable subject matter).

The case that is historically deemed to have decided the “copyrightability of computer programs” is the famed *Apple Computer, Inc. v. Franklin Computer Corporation* case. *Apple Computer, Inc. v. Franklin Computer Corp.*, 714 F.2d 1240 (3rd Cir. 1983). In the case, Franklin Computer was producing a clone of the Apple II computer and had copied both the Apple ROM and a number of computer programs from Apple Computer. Franklin Computer argued that Apple’s operating system programs were not protectable under copyright law. The Court held that Franklin Computer’s contention that operating system programs are *per se* not copyrightable was not persuasive. The relevance is that a computer program’s object code, which is more machine-oriented than the original source code version, should be copyrightable for software to be meaningfully protected (when outside of patents). In sum, the copyrightability of Bio-CAD files is unsettled. While the U.S. Copyright Office would allow for copyright registration for the source code of a Bio-CAD file for an applicant who would be

Bio-CAD file from being considered patentable subject matter, even before any disqualification for abstractness under 35 U.S.C. § 101.¹⁹⁹ While some commentators may argue that a Bio-CAD file would not be considered an entire human organism, a scan of any body part of a human may arguably be construed as being a human organism under the deficiencies of the Weldon Amendment of the AIA.²⁰⁰ Thus, unlike CAD files, which some commentators have argued cannot be patentable because they are software instructions,²⁰¹ Bio-CAD files may not be patentable subject matter under an ill-defined human organism exception.

The AIA could prohibit a Bio-CAD file from being patentable subject matter as a human organism. Moreover, assuming *arguendo* that somehow a Bio-CAD file did qualify under the AIA as patentable subject matter, the USPTO Interim Guidance²⁰² would prohibit the Bio-CAD file from being patentable subject matter for not exhibiting markedly different characteristics from a product of nature. Because the USPTO Guidance is based on *Myriad*, which held that DNA was the physical embodiment of information and of nature and, therefore, an unpatentable product of nature,²⁰³ then a Bio-CAD file as information content could similarly not be patentable subject matter.

A closer look at the Interim Guidance reveals the supporting reasoning. Under Step 1 of the Interim Guidance, a Bio-CAD file could conceivably be claimed as a tangible object as a component of a computer.²⁰⁴ The more pressing issue is the markedly different characteristics analysis. Under Step 2A of the USPTO's new markedly

willing to deposit the source code, the object code aspect of a Bio-CAD file would be unclear (unless it embodies the original expression). An applicant would have to state in writing to the U.S. Copyright Office that the work deposited as object code contained copyrightable authorship. It is well understood that reproductions of on-screen text, buttons, and commands, such as those being shown on a computer that displayed a Bio-CAD file, would not be appropriate as a substitute for a deposit for a source code deposit. However, whether or not the computer language encompassing a Bio-CAD file as written in some sort of scripted language would be equivalent to source code is unsettled and unclear, and could be the foundation of a separate Article.

199. 35 U.S.C. § 101 (2012).

200. See Torrance, *supra* note 102.

201. See Brean, *supra* note 2, at 841 (suggesting that there is a gap in patent law that does not account for patenting per se digital printable products because CAD files are similar to software and might be compared to a blueprinting or anything containing design information, such as a schematic, template, or prototype).

202. See *supra* notes 133–147 and accompanying text.

203. See CATO SUPREME COURT REVIEW: 2012–2013 279, 280 (Ilya Shapiro ed., 2013) (emphasizing the “information encoded in the DNA molecule” and discussing that in *Myriad* the “Court agreed . . . that DNA is primarily an information-carrying molecule” and “isolated DNA is *not* patent-eligible subject matter”); see also *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

204. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134, at 7.

different characteristics standard,²⁰⁵ Bio-CAD files would not possess markedly different characteristics from the object from which it is derived because it has identical structure, function, or properties to the biological object to be 3D bioprinted, but only in information content form. Regardless of whether the Bio-CAD file was created with a 3D modeling program or through the use of a 3D scanner, it would simply be a digital representation or device profile²⁰⁶ with information concerning the color and spatial aspects of the natural object. There would not be any difference in structure, function, and/or properties to justify a Bio-CAD file being markedly different from the natural object it represents. Even though other commentators have suggested that existing law will close the gap between the digital and tangible worlds and define patentable objects,²⁰⁷ Bio-CAD would arguably not have markedly different characteristics from the object found in nature.

Even under the subsequent Step 2B of the Interim Guidance, a Bio-CAD file would likely not be patentable subject matter under the “significantly more inquiry.”²⁰⁸ A Bio-CAD file would likely not fit any of the factors provided for in this step of the Interim Guidance. For example, a Bio-CAD file would not be an improvement to another technology, to the functioning of a machine, to effecting a transformation or reduction of a particular article, or to adding a specific limitation other than to what was understood. Each of these factors would cut against patent eligibility for a static Bio-CAD file that is simply a digital representation of a natural object.

Unlike static, unmodified Bio-CAD files that are based on MRI or CT scans, or are created in 3D modeling programs, other Bio-CAD files could be modified *in silico*.²⁰⁹ Bio-CAD files, which represent an element of a human organism in digital medical images, can also be exchanged in a marketplace that allows others to modify the models before 3D

205. *See id.* at 18.

206. While the Court in *Digitech* held that “data in its ethereal, non-physical form is simply information that does not fall under any of the categories of eligible subject matter under section 101,” when the technology at issue was “a device profile for describing properties of a device in a digital image reproduction system,” the fundamental issue is not whether claims are abstract ideas, but instead whether the invention is even patentable subject matter as a digital representation of a natural object. *Digitech Image Techs., LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344, 1349–50 (Fed. Cir. 2014).

207. *See Osborn, supra* note 19, at 1356 (suggesting that from an infringement standpoint, the interest in CAD files is not the files themselves but instead the object ultimately produced. Therefore, the reduced gap between digital and physical worlds considers CAD files to be the object itself, and the mere creation of the CAD file would constitute infringement by making or 3D printing the object.).

208. *See* 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134, at 18.

209. *See Biomedical Modeling Inc.: BioCad, supra* note 181.

bioprinting.²¹⁰ Bio-CAD files can also serve as preexisting modules that can be bought and downloaded before being transmitted to a 3D bioprinter to create a new aspect of an organism.²¹¹

Thus, Bio-CAD files not only converge digital and physical worlds, as with CAD files, they also converge living and nonliving worlds in a virtual environment. The convergence of living, nonliving, digital, and physical worlds with Bio-CAD files challenges patentable subject matter doctrine. Because of the convergence of so many technological domains, and the potentially added complexities with post-processing and integration,²¹² 3D bioprinting is more highly scrutinized than 3D printing,²¹³ and a more in-depth assessment of patentable subject matter would require identifying whether Bio-CAD has been modified or remains unmodified.

Because a Bio-CAD file can be modified by changing numerical parameters, calculating resulting geometries, and storing the models in repositories before post-processing 3D bioprinting steps,²¹⁴ living and nonliving parameters can be altered digitally. The ability to modify *in silico* alters the analysis of patentable subject matter with unmodified Bio-CAD files. For instance, a human organism element scanned into a Bio-CAD file could be modified *in silico* to remove or mask the human organism element, which may not be detected as containing any human organism element upon completion of the 3D bioprinting process. The removal of the human organism characteristic *in silico* could render the Bio-CAD file no longer a human organism, no longer falling under the AIA exception against human organisms. Additionally, the end result 3D bioprinted material would not fall under the AIA exception against human organisms.

In addition, under Step 2A of the USPTO's new "markedly different characteristics" standard,²¹⁵ a modified Bio-CAD file would likely be found to be patentable subject matter. Because a modified Bio-CAD file has new structure, function, and/or properties, it would be considered

210. See EMBODI3D, <http://www.embodi3d.com/> [<https://perma.cc/S46N-HD93>] (offering a website for users to share digital designs of anatomic structures).

211. *Digitizing Life: The New Frontier*, ATLANTIC COUNCIL (Dec. 6, 2013), <http://www.atlanticcouncil.org/blogs/futuresource/digitizing-life-the-new-frontier> [<https://perma.cc/47KK-9KEK>].

212. See *supra* notes 36–37 and accompanying text.

213. See Tran, *supra* note 6.

214. Mary-Ann Russon, *MIT Simplifies 3D Printing By Making It Easier to Modify 3D Models*, INT'L BUS. TIMES (Sept. 7, 2015), <http://www.ibtimes.co.uk/mit-simplifies-3d-printing-by-making-it-easier-modify-3d-models-1518781> [<https://perma.cc/G67F-3T3J>] (discussing a new, web-based software that makes it simpler for users to make modifications to 3D models in CAD files, such as 3D bioprinting CAD files, to print out quicker).

215. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134, at 18.

patentable subject matter. A modified Bio-CAD file would have different structure, function, and/or properties than the natural product from which it is based and, therefore, the end result printed object would also have different structure, function, or properties than the natural object because the modified Bio-CAD file is the equivalent of the printed object.

Thus, the Interim Guidance with the “markedly different characteristics” standard could produce different determinations of patentable subject matter for a Bio-CAD file based on whether it is modified or not. The development and growth of commercial exchanges to share Bio-CAD files makes it a challenge to track which file is modified and which is unaltered. For this reason, this Article proposes that the USPTO adopt a modified standard to supplement patent law’s “markedly different characteristics” examination of nature-based products in Part IV.

C. *Processed 3D Bioprinted Materials Should be Patentable Subject Matter*

At first glance, it can appear that 3D bioprinted living tissues (whether for organ transplants, *in vivo* skin repair, or wearable microbiomes) are nothing more than an assembly of cells organized in a 3D structure. However, 3D bioprinted tissues are manufactured by natural growth through intrinsic self-assembly principles found in nature.²¹⁶ In such cases, where nature is emulated inside of a 3D bioprinter, the resulting product would arguably not have markedly different characteristics because nature is directing the creation. However, human ingenuity is arguably the cause for the precision, automation, and deposition of the bioprint particles inside of a 3D bioprinter that produce 3D bioprinted materials.

In other cases, the assembly of 3D bioprinting cells would be combined with artificial materials, such that a mixed living and nonliving 3D bioprinted material would be achieved. The result is an easy case of markedly different characteristics because the infusion of artificial materials would structurally and visibly be considered markedly different. As a conceptual example, artificial materials, such as Kevlar™, could be introduced into a product of natural materials to be 3D bioprinted for *in vivo* skin repair.

A more difficult case is 3D bioprinted materials lacking any addition of artificial materials. Under the Interim Guidance, a manufacture of 3D

216. Karoly Jakab et al., *Tissue Engineering by Self-Assembly and Bio-Printing of Living Cells*, BIOFABRICATION, June 2010, at 1, 9, 10 (discussing that 3D bioprinting exploits intrinsic self-organizing principles of cells and tissues, natural vessel forming processes, and morphogenetic principles such as cell sorting and tissue fusion via automation of the deposition step that enables the building of 3D custom-shaped tissues and organs without the use of any scaffold).

bioprinted materials would be markedly different than the materials inputted in the 3D bioprinter, which would produce a material with a new form, structure, function, and/or property. The current state of 3D bioprinting—printing a scaffold, applying cells to the scaffold, and growing the culture of cells²¹⁷—provides a new form, quality, and properties to the cells. The resulting 3D bioprinted cells claimed as a manufacture would be markedly different²¹⁸ from the natural state of the material that is introduced into a 3D bioprinter as an input. Moreover, the composition of matter of the resulting 3D bioprinted cells when fused would have a new quality, whether caused by scaffold-based printing or scaffold-free printing,²¹⁹ through aggregation and perfusion from printing.²²⁰ Thus, 3D bioprinting materials inventions would possess physical characteristics that would qualify as patentable subject matter because such living organisms are no longer products of nature.

Inventors can avoid the patentable subject matter challenges with producing exact replicas by slightly modifying the 3D bioprinted object from what appears in nature. Any change in structure, function, or properties produced by the 3D bioprinting process specified in the patent specification²²¹ would deem the material patentable subject matter. Thus, the markedly different standard does not distinguish well between slightly modified and wholly modified 3D bioprinted materials. A clearer standard would prevent inventors from wasting time in attempting to slightly modify a prospective 3D bioprinting material to attempt to muster passing an unclear USPTO examination standard. Instead, an inventor's time could be better spent innovating, rather than attempting to engineer methods of slightly, but not fully, modifying products of nature through 3D bioprinting processes.

D. Post-Processing and Integration of 3D Bioprinted Materials is Unsettled

In certain situations, 3D bioprinted materials may contain markedly different characteristics than that found in nature, but may still be

217. LIJIE GRACE ZHANG ET AL., 3D BIOPRINTING AND NANOTECHNOLOGY IN TISSUE ENGINEERING AND REGENERATIVE MEDICINE 358 (1st ed. 2015).

218. 3D bioprinted living tissues and organs are significantly different from their human counterparts because there are structural differences between a 3D bioprinted organ and the parent organ brought about by laser-based writing, ink-jet based delivery, or extrusion-based deposition of cells. Thus, the physical 3D bioprinting process itself created new form, qualities, and properties of cells, and would be considered a manufacture.

219. See Bakhsinejad, *supra* note 25 (explaining bio-printing methods).

220. Ibrahim Ozbolat & Yin Yu, *Bioprinting Toward Organ Fabrication: Challenges and Future Trends*, 60 IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING 691, 696 (2013).

221. Phillips v. AWH Corp., 415 F.3d 1303, 1315 (Fed. Cir. 2005) (emphasizing the importance of the role of the patent specification as a source of meaning of patent claim terms).

considered human and not qualify as patentable subject matter under the AIA. The post-processing of 3D bioprinted materials can infuse living, human elements that can render what was a markedly different material from that found in nature with a mix of living and nonliving elements. The mixture of living and nonliving characteristics introduced by 3D bioprinting would further challenge patentable subject matter doctrine. The introduction of artificial materials during the final maturation process of a 3D bioprinted material would render the product a mixed living and nonliving material. For example, a 3D bioprinted kidney or heart could have vascularization enabled through artificial materials.

Where 3D bioprinting challenges patentable subject matter doctrine under the markedly different characteristics examination is the prospect of the technological advancement to the point where 3D bioprinted tissues and organs are indistinguishable from natural tissues and organs. When 3D bioprinted tissues and organs are identical in form and function to natural tissues and organs, then they would be considered naturally occurring. This reasoning has some basis in the current state of the art because 3D bioprinted organs are not yet populated with nerves and blood vessels in an exact replica fashion.

The state of the art of 3D bioprinted organ lacks nerves and vasculature, which are necessary for the viability and function of the organ.²²² Developments in 3D bioprinting are advancing to the point where nerves and blood vessels could be present. This exact replica dilemma in 3D printing is not far away. Would such a 3D bioprinted material be considered a human organism? Where would the world of nonliving stop and where would the world of a human organism start in this 3D bioprinting world? Would a 3D bioprinted material with markedly different characteristics than those found in nature be considered a human organism under the AIA?

These perplexing questions are further complicated when 3D bioprinted materials are integrated in a human organism. For instance, should 3D bioprinted wearable microbiomes that nourish the skin and repair damaged tissues be considered patentable subject matter?²²³ In such a case, an argument could be made that a wearable microbiome would be considered a 3D bioprinted material integrated into a human body and

222. Ozbolat, *supra* note 220, at 696 (specifying that the most critical challenge for 3D bioprinting is the integration of vascular networks, which allow 3D bioprinted organs to receive enough nutrients and enable gas exchange and waste removal).

223. *See supra* notes 53–57 and accompanying text.

therefore, as a method of medical treatment, would be exempt from being patentable subject matter.²²⁴

However, the integration of a 3D bioprinted material into a human organism could be performed during the process of 3D bioprinting itself. This could complicate patentable subject matter doctrine because the line between treatment and 3D bioprinting would be blurred. The integration of a 3D bioprinting material into a human being, even if the material retains its markedly different characteristics, can introduce a nonliving element into a human organism during the 3D bioprinting process. For example, 3D bioprinting can enable *in situ* and *in vivo*²²⁵ deposition operations to treat skin damage and enable wound healing.

3D bioprinting inkjet technology can easily be transported from patient to patient to rapidly print skin constructs of any cell type or biomaterial to treat burn victims *in situ* or provide artificial skin substitutes.²²⁶ Also, 3D bioprinting proof-of-concept development has shown the use of robotic arms with 3D bioprinting units that enter the body to automatically reconstruct new tissues and organs under the control of surgeons, utilizing *in vivo* bioreactors to facilitate the maturation of 3D bioprinted constructs.²²⁷ While *in vivo* 3D bioprinting combined with robot-assisted surgery is largely conceptual, it presents a pending patentable subject matter challenge.

The joining of an entire organ during 3D bioprinting might be considered too human and could be conceptually equivalent to a human organism, therefore disqualifying it from being patentable subject matter under the AIA. Taken to the extreme, the question arises—what if an entire human organism could be 3D bioprinted? As it stands, what can be considered a human organism under the AIA is unclear with respect to the continuum from living, to mixed living and nonliving, and to nonliving in 3D bioprinting.

224. 35 U.S.C. § 287(c) (2011); Fariba Sirjani & Dariush Keyhani, 35 U.S.C. § 287(c): *Language Slightly Beyond Intent*, 3 BUFF. INTELL. PROP. L.J. 13, 14–16, 35–37 (2005).

225. See *supra* note 38 and accompanying text.

226. Kyle W. Binder, *In Situ* Bioprinting of the Skin (May 2011) (unpublished Ph.D. dissertation, Wake Forest University Graduate School of Arts and Sciences), https://wakespace.lib.wfu.edu/bitstream/handle/10339/33425/Binder_wfu_0248D_10078.pdf?sequence=1 [<https://perma.cc/X6S3-9KLA>] (demonstrating in a nude mouse wound model that *in situ* 3D bioprinting is a viable technique for repair of full-thickness skin wounds, enabling virtually any cell type, macromolecule, or biomaterial to be directly 3D bioprinted onto a wound).

227. Manyi Wang et al., *The Trend Towards In Vivo Bioprinting*, 1 INT'L J. BIOPRINTING 15, 16–22 (2015) (demonstrating pilot studies of *in vivo* 3D bioprinting of *de novo* tissues and organs that are directly fabricated and positioned at a damaged site in a living body).

IV. U.S. PATENT LAW SHOULD EVOLVE ITS PATENTABLE SUBJECT MATTER ASSESSMENT

The emergence of 3D bioprinting prompts a need for a clearer standard for patentable subject matter for nature-based products in general and for 3D bioprinting specifically. The lack of guidance in the AIA's exemption of human organisms and the unclear markedly different characteristics standard for patentable subject matter of nature-based products, however, does not mean that either is incompatible with patenting of 3D bioprinting technology. Rather, what is needed is a clearer standard that provides inventors, the USPTO, and courts guidance on what may be patentable subject matter as 3D bioprinting applications stress the existing U.S. patent law regime.

Moreover, a clearer definition of what is or is not a human organism will also help to delineate patentable subject matter. The silent amendment to patentable subject matter in the AIA has added more confusion to what is patentable subject matter in light of the emergence of 3D bioprinting.²²⁸ A clearer definition of what is not a human organism and what is not nature are necessary for U.S. patent law to evolve and consider the advent of 3D bioprinting.

Clarifications on patentable subject matter are particularly important to enable inventors and patent practitioners to focus and expand upon their research, development, and patent filing strategy. Because the law governing the patentable subject matter requirements for years has been unclear,²²⁹ and it appears that it will remain unclear in the near future unless a new framework is adopted,²³⁰ it is possible that the validity of 3D bioprinting patents will be challenged.²³¹ Invalidity challenges to 3D bioprinting inventions could stifle commercialization of 3D bioprinting

228. See *supra* notes 153–168 and accompanying text.

229. Sarah Smith, *Claiming a Cell Reset Button: Induced Pluripotent Stem Cells and Preparation Methods as Patentable Subject Matter*, 56 B.C. L. REV. 1577, 1598 (2015) (suggesting that there has been an ongoing struggle in the courts to identify the boundaries of patentable subject matter, especially in the field of biotechnology); David O. Taylor, *Amending Patent Eligibility*, 50 U.C. DAVIS L. REV. 2149, 2154 (2017) (discussing that the Supreme Court has repeatedly failed to identify a patent eligibility standard and noting that the Supreme Court has been obsessed with non-statutory exceptions to patent eligibility, resulting in considerable confusion).

230. Efthimios Parasidis, *A Uniform Framework for Patent Eligibility*, 85 TUL. L. REV. 323, 329, 333 (2010) (proposing a decision tree algorithm that sets forth a series of questions on whether a patent claim is precluded from patent eligibility in light of a lack of a comprehensive test for determining patent eligible subject matter, which results in inconsistencies in district court rulings and within the U.S. Patent & Trademark Office).

231. A defense to a claim for patent infringement is that the patent is invalid for not being patentable subject matter or for another section of the Patent Act. While a patent is presumed valid under 35 U.S.C. § 282, one method of attack on a patent is to examine whether what has been patented is patentable subject matter through a motion to dismiss. Because an invalid claim cannot be infringed, an accused infringer could be off the hook for the alleged infringement.

inventions emerging from laboratories from becoming commercial realities and having a positive impact on healthcare.

A. *Shortcomings of the Markedly Different Characteristics Standard*

The markedly different characteristics standard serves as a starting point for evaluating the degree of alteration from a product of nature, but it only compares an invention to the natural product from which it was derived. This comparison is based on an ill-defined description of structure, function, and/or properties, which are only described through a list of examples provided in the USPTO's Interim Guidance.²³² None of these examples consider 3D bioprinting. The markedly different characteristics standard has three shortcomings that necessitate a new standard, one that accounts for the advent and growth in 3D bioprinting.

First, the markedly different characteristics standard's requirement to contain only a new structure, function, and/or property from a product found in nature would incentivize inventors to tailor inventions to comply with this requirement. 3D bioprinting technology is increasingly able to produce objects that resemble products of nature. In the case of 3D bioprinted organs for transplantation, research and development towards 3D bioprinting and integrating nerves and vascularized tissues will eventually yield exact replica organs for transplantation. If a court were to utilize the USPTO's markedly different characteristic standard to require that a tissue created in a laboratory must have a slight degree of dissimilarity to a naturally occurring tissue, then inventors would purposefully try to create a 3D bioprinted tissue that possesses a slight degree of dissimilarity. Requiring a markedly different characteristic could compromise the effectiveness of 3D bioprinted material for medical treatment for which replicated tissues or organs could be used. Tissues or organs that are intentionally 3D bioprinted to be dissimilar to a slight degree from a naturally occurring tissue or organ might not integrate well into the human body, or might not have consistent 3D bioprinting production, which could render medical treatment derived from 3D bioprinting less effective than with near exact replication.

Second, 3D bioprinting technologies have advanced greatly since the *Chakrabarty*²³³ decision in 1980 and have continued to expand rapidly since the *Myriad* decision in 2013,²³⁴ and the technologies can more closely replicate nature. Therefore, requiring an invention to hold

232. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

233. See generally *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

234. See generally *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

markedly different characteristics than nature would reduce inventors' incentive to innovate. This would be disadvantageous to innovation and slow advancements towards producing replica organs, which could be utilized for critical organ transplantation needs. Researchers and inventors can more easily replicate naturally occurring products that share characteristics with the invention at issue. Researchers' time in attempting to advance 3D bioprinting technology to create a beneficial 3D bioprinted tissue or organ should be utilized to benefit the public, not to make a slight modification to pass an unclear USPTO examination standard. A requirement that an invention hold markedly different characteristics from a product of nature causes disincentives to innovation in 3D bioprinting. Society should incentivize 3D bioprinting researchers to create inventions that mimic products of nature because such 3D bioprinting inventions have substantial healthcare benefits and utility.

Third, a requirement that an invention hold markedly different characteristics than nature is a greater legal challenge to patentable subject matter today than it was during the time of the *Chakrabarty*²³⁵ decision in 1980 and even the recent *Myriad*²³⁶ decision in 2013. Due to the rapid technological progress of 3D bioprinting in recent years, inventors can more easily produce 3D bioprinted materials that share characteristics with products of nature. Inventors and patent practitioners would have to spend substantially more time and effort in distinguishing 3D bioprinting inventions from products of nature now than in the past. The law has not kept up with rapid advancements in 3D printing, let alone with 3D bioprinting. It would cost society more in the form of time and energy of inventors and patent practitioners drafting and prosecuting patent applications to overcome the markedly different characteristics standard than it would if there were a clearer and more flexible standard for 3D bioprinting inventions. A clearer standard would allow inventors to foresee whether their inventions are patentable subject matter.

These reasons necessitate a clearer standard to assess patentable subject matter for nature based products, such as those enabled by 3D bioprinting. The lack of clear boundaries in this area of patent law leaves unclear whether 3D bioprinting inventions are patentable subject matter. A clearer standard for nature-based biotechnologies in general would also assist USPTO Examiners and judges in assessing whether 3D bioprinting inventions are patentable subject matter.

235. See generally *Diamond*, 447 U.S. 303.

236. See generally *Myriad Genetics*, 133 S. Ct. 2107.

B. *Proposed Mixed-Scanned-Transformed (MST) Standard*

The markedly different characteristics standard focuses on the extent of physical differences between modified items and their naturally occurring counterparts. The words used in this standard came from the *Chakrabarty*²³⁷ case of 1980, and hence, are based in an era tied to old technologies. The standard used for patentable subject matter for nature-based products should not be based on what biotechnologies *have been*, but instead should be broadly concerned with what biological technologies, such as 3D bioprinting, *could be* in the future. Moreover, the markedly different characteristics standard for patentable subject matter has been vague to the point where it could function as a categorical prohibition of some inventions.

Because the markedly different characteristics standard has shortcomings, and because courts have yet to utilize this standard for assessing patentable subject matter for 3D bioprinting, a clearer standard would encourage clarity in patent law. A clearer standard that is flexible enough to capture unknown technologies and avoid limitations tied to historical considerations would need to be forward looking and inclusive. A clearer standard that articulates a continuum of change from nature would allow a court the flexibility to construe change from nature as it deems proper for the circumstances. Such a new standard would also need to provide public notice with specificity to inventors regarding what inventions would qualify as patentable subject matter.

This Article proposes a new standard, a Mixed-Scanned-Transformed (MST) standard, for nature-based products to supplement the Interim Guidance.²³⁸ As a supplement, the MST standard would be an additional step in the examination of nature-based products. This new MST standard would encourage 3D bioprinting inventions and ensure that patent incentives are coextensive with the development of emerging 3D printing technologies. The proposed, supplemented MST standard is consistent with older standards that emphasize purification, isolation, and markedly different characteristics of nature-based products but is not limited to only physical transformation based on chemical processes covered by the older tests on nature-based products. The proposed MST standard would also encompass other commentators' suggestions to compare structural and molecular properties²³⁹ in assessing patentable subject matter for nature-based products, as well as account for Bio-CAD files as patentable subject matter. The recognition that Bio-CAD files,

237. See *Diamond*, 447 U.S. at 309.

238. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

239. See Samantak Ghosh, *Gene Patents: Balancing the Myriad Issues Concerning the Patenting Natural Products*, 27 BERKELEY TECH. L.J. 241 (2012).

whether unmodified or modified, constitute patentable subject matter under the proposed MST standard means that additional 3D bioprinting inventions may qualify for patent protection.

In this proposed, supplemental “Mixed-Scanned-Transformed” standard, the word “mixed” refers to combining elements, which may include natural with non-natural elements, such as a product of nature with a man-made material. The word “scanned” refers to converting a physical object into a digital representation, such as in a medical image. The word “transformed” refers to making changes to a CAD file digitally, such as in a digital transformation through a computer, or to making changes physically, such as changing physical properties through a chemical process. Thus, transformed could indicate a change from physical to digital, or from digital to physical. The proposed, supplemental MST standard considers a product that is mixed, scanned, *or* transformed to qualify as patentable subject matter; it does not necessarily require a product to be mixed, scanned, *and* transformed to be patent eligible. For example, the MST standard would consider each of the following patentable subject matters: (1) mixed artificial and human biological materials, (2) scanned objects in a Bio-CAD file, and (3) information or data content that is transformed from the digital realm to the physical realm in the form of a product or material, or alternatively, a product or material that is transformed from the physical realm to the digital into information or data content.

There are two key differences between the markedly different characteristics standard and this newly proposed, supplemental MST standard. First, the Interim Guidance refers to markedly different characteristics being a change in structure, function, and/or properties.²⁴⁰ But such a change does not account for man-made materials that mimic nature. For example, there would be no differentiation between a synthetic material introduced into a 3D bioprinting process that mimics nature and a natural material that is 3D bioprinted that similarly mimics nature. In both cases, the structure, function, and/or properties would be the same, but the markedly different characteristics standard would not account for the fact that one is based on a product of nature and another a mixed synthetic and natural product. The markedly different characteristics standard has not been able to keep pace with 3D bioprinting’s ability to mix synthetic and natural materials.

Second, the markedly different characteristics standard presented in the Interim Guidance implies a change in structure, function, and/or properties either as a chemical change or physical change based on a

240. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

chemical process.²⁴¹ Would a change from a physical object to a digital object, in the form of a MRI or CT scan into a Bio-CAD file, be considered a markedly different characteristic in structure, function, and/or property? Would a Bio-CAD file modification, which would demonstrate a change digitally in structure, function, and/or properties to a 3D bioprinted object a press of a button away be considered markedly different? The intention of the Court in the *Myriad*²⁴² case does not account for the blurred physical-digital and blurred living and nonliving worlds of 3D bioprinting. A patentable subject matter standard, such as the proposed, supplemental MST standard, will consider Bio-CAD files equally important to other 3D bioprinting inventions, such as the 3D bioprinter and the 3D bioprinted material.

Accordingly, the proposed, supplemental MST standard would enable a 3D bioprinting inventor to provide reasoning to overcome disqualifications following the markedly different standard and significantly more inquiry, allowing the inventor to present arguments that describe the invention as mixed, scanned, or transformed. By supplementing the USPTO examination of nature-based products, this new examination step would give a patentee an opportunity to demonstrate that the invention has been mixed, scanned, or transformed. The proposed, supplemental MST standard would be adequately flexible to cover a continuum of degree of changes from nature and provide a sliding scale approach to assessing patentable subject matter for nature-based products.

C. *Responding to Potential Criticisms of the MST Standard*

This Article anticipates that some will critique the proposed, supplemental MST standard. Criticism of the proposed, supplemental MST standard will likely center on three main arguments: 1) the proposed standard may seem to violate the uniformity principle in patent law of not favoring certain technologies; 2) some may question whether the cloning decision in the case *In re Roslin Institute*²⁴³ would argue against patent eligibility of 3D bioprinting inventions; and 3) legal scholars may question whether a clearer standard for patentable subject matter for nature-based products incentivizes inventors. There have been many discussions on whether patents incentivize innovation and that is outside the scope of this Article. Instead, the first concern regarding the uniformity principle and the second concern regarding cloning are legitimate issues that would need to be addressed by Congress and the USPTO before implementing the

241. *Id.*

242. *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013).

243. *In re Roslin Institute (Edinburgh)*, 750 F.3d 1333, 1334 (Fed. Cir. 2014).

proposed, supplemental MST standard in the examination of nature-based patents, such as those of 3D bioprinting, at the USPTO.

1. Replying to Concerns on Uniform Treatment of Technologies in U.S. Patent Law

An improvement to the patentable subject matter standard for nature-based products should be the objective of each of the inventors who file patent applications, the USPTO and patent examiners, and the federal courts. A challenge with developing a clearer standard for biotechnological inventions, however, is the notion that U.S. patent law does not differentiate among technologies. The notion that the U.S. patent system operates as a uniform system that applies neutrally to all inventions has been contested by many commentators. Professors Dan Burk and Mark Lemley have suggested that there is an increasing divergence between patent law and the application of patent law to different industries, particularly with biotechnology.²⁴⁴ Another commentator has suggested that some provisions of the AIA are specific to certain types of inventions demonstrating a number of exceptions to technology neutrality.²⁴⁵

This Article does not debate whether sector-specific patent principles are merited or imprudent. The discussion herein does not delve into whether the patent system should operate as a uniform and neutral system to all inventions. Instead, this Article recognizes that the AIA has determined that there are limits to patenting human organisms. This limitation demonstrates that the congressional intent in the patent system is to have a different standard for patentable subject matter. Thus, there is impetus for modifying the U.S. patent system to work in a non-neutral fashion to meet the needs of specific industries where human organisms are at issue. The salient distinction of human organisms implies that the U.S. patent system may need to be tailored to reflect the needs of distinct technology sectors, such as 3D bioprinting, where inventions concerning human organisms are available and proliferating.

The proposed, supplemental MST standard more clearly addresses the rationale behind requiring that a nature-based invention possess a markedly different characteristic from the natural product from which it was derived. This Article suggests that the proposed, supplemental MST

244. Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH L.J. 1155, 1156–95 (2002) (suggesting there is variance in patent law because of the Person Having Ordinary Skill in the Art standard (PHOSITA), which generates a technology-specific body of patent law).

245. JOHN R. THOMAS, CONG. RES. SERV., R43264, TAILORING THE PATENT SYSTEM FOR SPECIFIC INDUSTRIES 7-5700, at 1 (2015) (noting that the AIA has limited patents on tax strategies and human organisms, has created proceedings that apply exclusively to patents pertaining to business methods, and prioritizes examination of applications important to national security).

standard will follow patent law's uniformity principle, which requires that all inventions be assessed equally regardless of technology specificity because it supplements the Interim Guidance. In other words, the MST assessment is simply an additional new Step 3 for the Interim Guidance²⁴⁶ and would only be applicable in the case an invention does not qualify under Step 2A's markedly different characteristics standard and under Step 2B's significantly more inquiry. This new Step 3 adds more clarity, and perhaps more complexity, to the USPTO's existing examination procedure, but it does not attempt to differentiate between technologies. Only if an invention does not qualify under Step 2A and Step 2B would such an invention even be considered under the newly proposed, supplemental MST standard. This Article argues that the proposed, supplemental MST standard is not meant to be a filtering and separating mechanism between various technologies, but instead, is meant to be a better means for delineating a boundary for determining what may or may not be patentable subject matter.

2. Distinguishing Cloning with Dolly the Sheep

In *In re Roslin Institute*, the court held that the patent claims directed to Dolly the Sheep²⁴⁷ were not patent eligible because a cloned animal "is an exact genetic replica of another [animal] and does not possess 'markedly different characteristics' from any farm animals found in nature."²⁴⁸ Dolly the Sheep had nucleic genetic material that was a copy of the adult from which she was cloned, and the word "clone" in the patent claims indicated an exact genetic identity.²⁴⁹ The patentee Roslin Institute had argued that Dolly the Sheep had phenotypic differences and had differences in mitochondrial DNA.²⁵⁰ Despite the patentee's arguments that the sheep did have phenotypic or mitochondrial differences, the Federal Circuit held that such differences were not claimed in the patent

246. See 2014 INTERIM GUIDANCE ON PATENT SUBJECT MATTER ELIGIBILITY, *supra* note 134.

247. U.S. Patent Application No. 09/225, 233 claimed the cloned animals included: "155. A live-born clone of a pre-existing, non-embryonic, donor mammal, wherein the mammal is selected from cattle, sheep, pigs, and goats. 164. The clone of any claims 155-159, wherein the donor mammal is non-foetal." *In re Roslin Institute (Edinburgh)*, 750 F.3d at 1335.

248. *Id.* at 1337 (citation omitted) (holding that the first mammal ever cloned from an adult somatic cell, Dolly the Sheep, was ineligible for patent protection as claimed because it constituted a natural phenomenon that did not possess markedly different characteristics than found in nature because the cloned sheep was an exact copy of the mammal from which the somatic cell was taken).

249. Jason Rantanen, *Claiming Clones*, PATENTLY-O (May 8, 2014), <https://patentlyo.com/patent/2014/05/claiming-clones.html> [<https://perma.cc/UJF2-VNP8>].

250. Donald Zuhn, *Dolly the Sheep Not Patent Eligible Subject Matter*, PATENT DOCS (May 8, 2014), <http://www.patentdocs.org/2014/05/in-re-roslin-institute-fed-cir-2014.html> [<https://perma.cc/E64H-XCF4>] (discussing that the Roslin Institute had argued clones should be patent eligible because the DNA originated from the donor oocyte rather than the donor nucleus).

claims, which were drafted in terms of genetic identity.²⁵¹ The court appeared to ignore that a clone would inherently have phenotypic differences due to its development in different environmental conditions than the donor.

One argument to distinguish 3D bioprinting from Dolly the Sheep is based on inept patent claims drafting. The patent claims directed to Dolly the Sheep failed to distinguish cloning in any way in the patent claims or the patent specification.²⁵² The court appeared to leave the door slightly ajar for patent eligibility of cloned sheep in stating:

There is nothing in the claims, or even in the specification, that suggests that the clones are distinct in any relevant way from the donor animals of which they are copies. The clones are defined in terms of the identity of their nuclear DNA to that of the donor mammals . . . the claims do not describe clones that have markedly different characteristics from the donor animals of which they are copies.²⁵³

The court's reasoning suggests that the unique features of the claimed sheep were not indicated in the patent claims, and therefore, the claims did not establish any differences from nature. The court seemed to indicate that better patent claims drafting could have highlighted the differences from nature and, therefore, may have enabled patent eligibility consideration of features that may have been markedly different from nature. In essence, the court seemed to implicitly interpret the claims in a manner least favorable to the patentee, whereas the USPTO's patent examiners would be charged with the broadest reasonable interpretation²⁵⁴ of such patent claims, which means the patent claims may have been patentable subject matter.

A second argument to distinguish 3D bioprinting from Dolly the Sheep is based on biology. Dolly the Sheep had shorter telomeres than other animals of the same age.²⁵⁵ Therefore, Dolly would not be considered an exact replica of her donor and, hence, would have the necessary markedly different characteristics to be considered patentable subject matter. This subtle difference of shorter telomeres, which was overlooked

251. See Rantanen, *supra* note 249.

252. See *In re Roslin Institute (Edinburgh)*, 750 F.3d at 1337.

253. See *id.* at 1339.

254. MPEP, *supra* note 65, § 2111 (specifying that during patent examination, patent claims must be given their broadest reasonable interpretation consistent with the specification, which is based on the Federal Circuit's *en banc* decision in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005)).

255. Mercedes K. Meyer, *Alice Sat on Prometheus and Met Dolly the Sheep Who Said Baaaaahhhh to Myriad*, AM. INTEL. PROP. L. ASS'N (Oct. 22, 2014), <http://studylib.net/doc/9811309/myriad—american-intellectual-property-law-association> [<https://perma.cc/KH9D-SDLL>] (indicating that telomeres, which are pieces of DNA that protect ends of chromosomes, shorten as cells divide and therefore considered as a measure of ageing of cells).

by the court and resulted in Dolly the Sheep's early death, would only have occurred in older sheep.²⁵⁶ Such a biological example is a type of difference that would have yielded markedly different characteristics. Because cloning does not produce an exact replica biologically, even if the patent claims attempt to claim as such, the inherent biological limitations of cloning would produce markedly different characteristics. A wise patent practitioner would attempt to capture such inherent biological differences in a patent claim. Similarly, any such biological differences promoted by 3D bioprinting technology would yield markedly different characteristics to result in patentable subject matter. 3D bioprinting technology itself has technological limitations that inherently would yield similar biological differences. Moreover, 3D bioprinting technology would enable precision design to create engineered differences in biology, and such a design choice would yield markedly different characteristics than what is found in nature.

V. SOUND POLICY FAVORS CLEARER PUBLIC NOTICE OF 3D BIOPRINTING

Throughout U.S. history, patentable subject matter doctrine has been flexible and robust by adapting to new technologies in diverse industries.²⁵⁷ Each time there is an emerging technology, the question of patent eligibility of a category of inventions is, at a fundamental level, a question about whether the benefits outweigh the costs that arise from granting patents to that category of invention.²⁵⁸

The utilitarian point of view of the patent system²⁵⁹ would support favoring the benefits of a new category to make available to the public new and useful inventions that would not otherwise have been available. To achieve this goal, a standard for determining patent eligibility of a new category would need to encourage (1) creation of inventions, (2) disclosure of inventions to the public, and (3) further development and commercialization of inventions.²⁶⁰ This Article contends that patentable subject matter standards for nature-based products should respond with a

256. *Id.*

257. See generally David J. Kappos et al., *A Technological Contribution Requirement for Patentable Subject Matter: Supreme Court Precedent and Policy*, 6 NW. J. TECH. & INTELL. PROP. 152 (2008).

258. Yuqing Cui, *A Quantitative Approach to Determining Patentable Subject Matter* (May 2015) (unpublished research paper, Harvard Law School) (on file with author).

259. See generally David S. Olson, *Taking the Utilitarian Basis for Patent Law Seriously: The Case for Restricting Patentable Subject Matter*, 82 TEMP. L. REV. 181 (2009) (suggesting that the U.S. Constitution and patent law casebooks indicate that our patent system incentivizes the production and distribution of innovation).

260. See John M. Golden, *Principles for Patent Remedies*, 88 TEX. L. REV. 505, 510–11 (2010).

more bright-line standard. By redrawing the patentable subject matter boundaries for nature-based products, new discoveries of 3D bioprinting materials and the Bio-CAD files that digitally represent them will promote clearer patenting. This will not necessarily lead to more patents being filed for 3D bioprinting inventions, but instead will lead to less ambiguity regarding what may be patentable in this emerging industry.

A clearer standard for patentable subject matter for nature-based products and for 3D bioprinting inventions would provide a clearer “notice function” and reduce the risks of disputes and litigation.²⁶¹ A clearer boundary of what may be considered patentable subject matter has an economic value to inventors for determining when to pursue patents, to the USPTO for its role as an agency in the examination of patent applications, and to the public for providing notice on what may be patentable.²⁶² The adoption of a more bright-line standard would give 3D bioprinting researchers a better indication of whether their inventions are patentable subject matter. This, in turn, would allow them to focus on improving 3D bioprinting, rather than patent attorneys and patent agents focusing on cleverly drafting patent claims²⁶³ in an attempt to qualify inventions under the markedly different characteristics standard.

Sound public policy favors that 3D bioprinting not be subject to ambiguous patent law standards, which can produce wasteful efforts to evaluate and enforce patent rights. Ambiguous patent law standards can lead to curtailment of invention activities due to threats of patent invalidity challenges and patent litigation enforcement.²⁶⁴ Rather than have the scope of 3D bioprinting patent rights be rendered obscured by uncertain patentable subject matter standards, more clarification and consistency of patentable subject matter would provide the impetus for development of 3D bioprinting inventions. A lack of clarity around the patentable subject

261. See JAMES BESSEN & MICHAEL J. MEURER, *PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK* 1, 6–10 (2008) (comparing patents to tangible property, each providing partial use and ownership rights and incentives to invest in acquisition, development, and maintenance; further stating that property systems fail to provide incentives when their validity is uncertain, and then when rights are highly fragmented or boundaries of rights are not clear and predictable, negotiations become cost prohibitive).

262. Alan Marco et al., *Patent Claims and Patent Scope 5* (USPTO, Economic Working Paper No. 2016-04, 2016), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2844964 (discussing that patent boundaries that are clearly defined to the benefit of the patent owner, the courts, third parties, and the public at large, give inventors and investors the confidence in taking the risk necessary to launch products and start businesses, as well as give the public at large the benefit of knowing precise boundaries of an exclusionary right).

263. See generally Tun-Jen Chiang, *Forcing Patent Claims*, 113 MICH. L. REV. 513 (2015) (suggesting that because patent claims define the scope of a limited monopoly right, patentees subtly slant the patent claim’s language in a way that aggrandizes their patent rights).

264. Keith E. Witek, *Developing a Comprehensive Software Claim Drafting Strategy for U.S. Software Patents*, 11 BERKELEY TECH. L.J. 363, 366–67 (1996).

matter standard would impose a disincentive to investing in emerging technologies such as 3D bioprinting. Moreover, patent quality would deteriorate when patent boundaries, such as those for patentable subject matter, are difficult to determine, thereby further causing societal loss.

Several relevant stakeholders would benefit from a clearer standard. A more bright-line standard for 3D bioprinting would be highly important for administrative, judicial, and private law contexts, as well as for overall public benefits. In an administrative context, clearer 3D bioprinting patentable subject matter would benefit inventors and USPTO examiners. First, 3D bioprinting inventors need a more bright-line standard to shape their patent claims so as to include the necessary features to qualify for patents. Second, USPTO patent examiners need a clearer standard to ensure consistency in accepting or rejecting patent claims covering new 3D bioprinting inventions. There will be reduced patent quality if USPTO patent examiners have difficulty properly reviewing patent applications.

Third, in a judicial context, federal courts called upon to enforce patents covering 3D bioprinting inventions will need clearer standards to determine, which, if any, 3D bioprinting patent claims are valid and enforceable. These judicial assessments of patent invalidity due to non-patentable subject matter will not only determine monetary and injunctive relief but will also indicate to potential infringers what patent licenses are necessary to use inventions or develop design-around patenting strategies. Thus, the definiteness of a 3D bioprinting standard affects interpretation by an initial court, inevitably affecting downstream litigation and licensing settlement negotiations.

Fourth, in a private law context, investors, such as angel investors or venture capitalists, need more clarity concerning patentable subject matter to shape investments in nascent, high-growth, startup companies that will develop and commercialize 3D bioprinting technologies. There will be greater societal costs if boundaries are not adequately delineated, such as investors needing to seek expensive legal opinions about patent boundaries and the scope of patent rights.²⁶⁵ 3D bioprinting startups, such as Organovo²⁶⁶ and Poietis,²⁶⁷ which have engaged in joint development agreements and partnerships with established companies, need clearer standards to assess the validity of 3D bioprinting patents as they transfer

265. See BESSEN & MEURER, *supra* note 261 (discussing that poor property notice would cause investors to more strongly consider their risk of being sued for patent infringement over the reward they might reap from owning and commercializing patents, and therefore without clear boundary markers, investors may not attempt to clear the necessary rights before investing).

266. See *Organovo Investor Presentation*, *supra* note 49.

267. See Cosimo, *supra* note 51.

their patent rights while also scaling their laboratory results with existing manufacturing and supply chains.

Fifth, established biomedical and biotech corporations will not only consider the validity of startups' patents in partnership agreements but will also consider whether to channel their own resources and budgets towards 3D bioprinting internal research and development and patenting efforts. In sum, private law transactions involving activities or products dependent on 3D bioprinting patents need to be able to predict whether the patents involved will be enforceable or an impediment to commercial strategies.

Sixth, and perhaps most importantly, organ transplantation hopefuls²⁶⁸ and burn victims²⁶⁹ are awaiting healthcare innovations for their medical needs. Slowing the rate of 3D bioprinting patenting will only prolong the shortage of organ transplantation and burn victim treatments. Patentable subject matter standards not only have an important role in patent law but also in health law. The standard for patentable subject matter is not only a gatekeeper function for patent law, but also indirectly serves as a gatekeeper for healthcare innovations. In essence, changes in patentable subject matter affect whether a patent will be valid and whether inventions will be commercialized. In sum, a broad view of patentable subject matter for 3D bioprinting does not automatically mean there will be a large number of 3D bioprinting patents. Rather, recognizing that 3D bioprinting innovations constitute patentable subject matter will lead to heightened patenting, thereby enabling easier patent examination by the USPTO, clearer and higher quality issued patents, and quicker-to-commercialize encompassing technologies. The promise and incentive of patent rewards will encourage 3D bioprinting innovation and invention concerning patentable subject matter. The choice of which categories of 3D inventions to allow into the patentable subject matter boundaries is essentially a choice of which healthcare innovations the patent system should promote. A more bright-line approach to patentable subject matter will ensure that patent incentives will coexist with the scope of potentially beneficial associated public healthcare solutions.

The demarcation of patentable subject matter boundaries for an emerging technology is not an easy task.²⁷⁰ This Article provides a first

268. See Harbaugh, *supra* note 42.

269. Illene Wolff, *The Next Step for Bioprinting: 3D Printing Skin*, ADVANCED MANUFACTURING (Mar. 7, 2016), <http://advancedmanufacturing.org/next-step-bioprinting-3d-printing-skin/> [<https://perma.cc/8GHB-CQGE>] (stating that there are 11 million burns annually worldwide that need medical attention according to the World Health Organization, and that in the U.S. in 2015, 486,000 burn injuries received medical treatment according to the American Burn Association).

270. See BESSEN, *supra* note 261 (describing that unlike tangible property, which is a rival good because only one person can use it at a time, more than one person can use an invention, and therefore, while patent law shares some doctrinal features in common with tangible property, the boundaries of

step towards providing more clarity around the patentable subject matter boundaries for emerging 3D bioprinting technologies. A clearer standard for patentable subject matter will not necessarily mean more patenting of 3D bioprinting inventions, but will help avoid downstream, costly disputes and lead to more rapid growth of the emerging 3D bioprinting industry.

CONCLUSION

Inventors are combining principles of 3D printing with synthetic biology to replace damaged tissues, restore malfunctioning organs, permit organ transplantation, repair skin burns, and create wearable microbiomes. This new phenomenon of 3D bioprinting blurs the digital, physical, living, and nonliving worlds, and challenges U.S. patent law in the patentable subject matter doctrine. The transformative technology of 3D bioprinting magnifies the unclear markedly different characteristics standard and human organism exception in U.S. patent law. These shortcomings require that U.S. patent law respond with a more bright-line standard to promote 3D bioprinting inventive activity. A proposed supplement to the current USPTO examination procedure would lead to clearer 3D bioprinting patenting and promote administrative, judicial, and private law efficiencies and healthcare benefits.

patent law doctrines are tougher to define than those of real property because multiple inventors may have rights to an invention that could have many different facets).